NUMBER 104 May 2020

# CODE OF PRACTICE REVIEW

PMCPA | Prescription Medicines Code of Practice Authority

The Prescription Medicines Code of Practice Authority (PMCPA) was established by The Association of the British Pharmaceutical Industry (ABPI) to operate the ABPI Code of Practice for the Pharmaceutical Industry independently of the ABPI. The PMCPA is a division of the ABPI which is a company limited by guarantee registered in England & Wales no 09826787, registered office 7th Floor, Southside, 105 Victoria Street, London SW1E 6QT.

## PUBLIC REPRIMAND FOR ASTRAZENECA

AstraZeneca UK Limited has been publicly reprimanded by the Code of Practice Appeal Board for failing to provide complete and accurate information in an open and transparent way (Case AUTH/3013/1/18).

In Case AUTH/3013/1/18, the Code of Practice Panel ruled breaches of the Code as an AstraZeneca advisory board which was held outside the UK, in November 2017, and involved UK delegates had not been certified. AstraZeneca accepted the Panel's rulings and provided the requisite undertaking.

Following completion of the case in April 2018 and its publication on the PMCPA website in May, the PMCPA received further information in June which appeared to come from the original anonymous, non-contactable complainant who had described him/herself as an AstraZeneca employee. The further information was a high level internal email regarding options for dealing with the advisory board at issue. AstraZeneca provided a response and additional information.

The Panel reconvened to consider the additional information and concluded that on balance it would not make a formal report to the Appeal Board on this occasion despite its concerns about AstraZeneca's approach to the provision of information. The impression of the additional email was that the UK company had concerns about the arrangements for the advisory board, in particular the number of AstraZeneca attendees. Full details about the number of AstraZeneca attendees had only been provided when the Panel had asked for further information. The Panel's view was that the additional information now provided would not have changed its ruling of no breaches of the Code.

The Appeal Board was provided with details of the Panel's further consideration in a similar format to the details provided when cases concluded at Panel level in accordance with Paragraph 13.4 of the Constitution and Procedure. Copies of relevant material including the update to the case report were also provided.

The Appeal Board considered that the additional information raised serious issues including about the provision of incomplete and/or inaccurate information. The Appeal Board's view was that further consideration should be given to this matter including the possibility of imposing further sanctions under Paragraph 11.1 of the Constitution and Procedure. AstraZeneca was invited to comment and, at its subsequent consideration of the matter, the Appeal Board noted that the additional email was clearly central and relevant to this case and did not appear to be consistent with other material previously provided. In the Appeal Board's view, to not submit the email was inexplicable. Effective self-regulation required companies to be open and transparent when responding to complaints; they had a duty to disclose all relevant documents and information. The Appeal Board was not satisfied with AstraZeneca's submission as to why it had not provided the email when responding to the complaint.

The Appeal Board considered that the email should have been provided to the PMCPA as part of AstraZeneca's response. Notwithstanding AstraZeneca's submission that it had now updated its processes, the Appeal Board noted that self-regulation relied, *inter alia*, upon the provision of complete and accurate information from pharmaceutical companies.

The Appeal Board was concerned to note that AstraZeneca was also publicly reprimanded in 2016 for providing inaccurate information to the Panel (Case AUTH/2793/9/15).

Full details of Case AUTH/3013/1/18 can be found on page 82 of this issue of the Review.

## FURTHER PUBLIC REPRIMAND FOR OTSUKA EUROPE

In Case AUTH/3041/6/18 and Case AUTH/3123/11/18, the Code of Practice Appeal Board was very concerned about the potential patient safety implications arising from Otsuka Europe's failure to implement timely changes in certain summaries of product characteristics (SPCs) and make consequential changes to its promotional materials. The Appeal Board decided, in both cases, to publicly reprimand the company (see May 2019 Code of Practice Review).

In addition to the public reprimands above, the Appeal Board also decided to require, with regard to each case, an audit of Otsuka Europe's procedures in relation to the Code. On receipt of the audit reports, the Appeal Board was very concerned to note the extent of the company's failings and that Otsuka Europe had previously not provided it with accurate information. The Appeal Board noted that self-regulation relied, inter alia, upon the provision of complete and accurate information. The Appeal Board decided that, in Case AUTH/3041/6/18 and Case AUTH/3123/11/18, Otsuka Europe should be additionally publicly reprimanded for providing inaccurate information to the Appeal Board.

Full details of the two cases can be found on the PMCPA website.

## CODE OF PRACTICE TRAINING

Training seminars on the Code of Practice, run by the Prescription Medicines Code of Practice Authority and open to all comers, are held on a regular basis in central London.

These full day seminars offer lectures on the Code and the procedures under which complaints are considered, discussion of case studies in syndicate groups and the opportunity to put questions to the Code of Practice Authority.

For dates of the Code of Practice Seminars in 2020 please see the PMCPA website.

Short training sessions on the Code or full day seminars can be arranged for individual companies, including advertising and public relations agencies and member and non member companies of the ABPI. Training sessions can be tailored to the requirements of the individual company.

*For further information regarding any of the above, please contact Nora Alexander for details (020 7747 1443 or nalexander@pmcpa.org.uk).*

## HOW TO CONTACT THE AUTHORITY

Our address is:
Prescription Medicines Code of Practice Authority
7th Floor, Southside, 105 Victoria Street, London SW1E 6QT

www.pmcpa.org.uk

Telephone: 020 7747 8880

Copies of the Code of Practice for the Pharmaceutical Industry and of this Review can be obtained from Lisa Matthews (020 7747 8885 or lmatthews@pmcpa.org.uk).

Direct lines can be used to contact members of the Authority.

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|---|---|
| Heather Simmonds: | 020 7747 1438 |
| Etta Logan: | 020 7747 1405 |
| Tannyth Cox: | 020 7747 8883 |

The above are available to give informal advice on the application of the Code of Practice.

The Authority rather than the ABPI is the contact point for information on the application of the Code.

**CASE AUTH/2780/7/15**

# ANONYMOUS, NON-CONTACTABLE EMPLOYEE v ASTELLAS

## False response and further failure to provide accurate information

**An anonymous and non-contactable complainant who appeared to be an employee of Astellas complained about the truthfulness of Astellas's response to Case AUTH/2747/1/15 which concerned the arrangements for an Astellas Pharma Europe meeting held in Milan in February 2014. In that case the company was ruled in breach of the Code including Clause 2 and was required by the Appeal Board to issue a corrective statement to all UK attendees.**

**The complainant stated that Astellas colleagues recently provided training on the outcome of Case AUTH/2747/1/15 and its learnings and a 'town hall' meeting was convened, where a very senior employee (identified by job title) of Astellas Pharma Europe discussed the matter, albeit in a very dismissive manner.**

**The complainant stated that it was extremely alarming and concerning that the account given to the PMCPA was knowingly false and intentionally misleading. In its response to Case AUTH/2747/1/15 Astellas claimed that all invitees were identified and grouped based on their 'clinical expertise' and 'experience of treating patients with mCRPC' (metastatic castration – resistant prostate cancer). Unfortunately, nothing was further from the truth and Astellas knew that but deliberately chose to conceal it from the PMCPA. The complainant provided a copy of the briefing given by Astellas to its affiliates which stated that all 30 opinion leaders chosen by each affiliate had to be; 'mid to top level opinion leaders with the potential to be local product champions'. Furthermore it was requested that they be 'data naïve'. The complainant alleged that this directly contradicted the claim made that they be chosen based on their clinical expertise.**

**The complainant stated that it was also disappointing that Astellas had still not learnt from rulings of breaches of the Code including Clause 2, and that the company had deliberately misled the PMCPA about a very serious complaint. The complainant urged the PMCPA to consider more serious sanctions including an audit of the company's procedures, a public reprimand and possible suspension or exclusion from membership of the ABPI.**

**The detailed response from Astellas Pharma Europe is given below.**

**The Panel noted the outcome of Case AUTH/2747/1/15 and that the Panel had ruled Astellas Europe in breach of the Code including Clause 2 in relation to arrangements for a meeting.**

**The Panel had also reported the company to the Code of Practice Appeal Board. The Panel's rulings were not appealed. The Appeal Board required Astellas Europe to issue a corrective statement to UK attendees. This was issued on 1 July 2015.**

**The Panel noted that the meeting at issue in Case AUTH/2747/1/15 had been run by Astellas Europe. The complaint concerned arrangements for UK attendees. In this regard the Panel noted that Astellas UK was responsible for the acts/omissions of its affiliates including its UK based European headquarters. In the Panel's view this remained the position even if the UK based European affiliate had responded directly to the complaint. In its response to Case AUTH/2780/7/15 Astellas Europe explained that Astellas UK and Astellas Europe had decided that the European affiliate should respond to the complaint. Correspondence in relation to Cases AUTH/2747/1/15 and AUTH/2780/7/15 had consequently been sent directly to Astellas Europe. The Panel noted the company's submission about the involvement of the UK company with the response to Case AUTH/2747/1/15 prepared by Astellas Europe. The Panel noted the position of Astellas UK in relation to the present complaint remained as set out above.**

**The Panel noted that the criteria used to select advisory board members to attend the meeting in question must stand up to scrutiny and relate solely to their ability to provide expertise to the company. The Panel considered that three emails sent in September 2013 and October 2013 were wholly unacceptable in relation to the criteria to be used to identify potential advisory board members. All the emails and/or their attachments listed above referred to invitees being-mid to top level product opinion leaders with the potential to be local product champions within the relevant market and data-naïve customers ie those who had not been involved in any Astellas Europe or national/local advisory board meetings prior to the Pan EU Expert Meeting.**

**A presentation to the Oncology Steering Committee (5 February 2013) referred to the success of the Pan – European Uro-oncology Advisory Board held in Barcelona in November 2012. It stated that the proposed structure of future meetings was discussed/agreed by a UK medical employee. This presentation referred to the aims and suggested target audience for 13/14 pan European advisory board meetings as:**

**'Objectives for meeting**

- **Increase Astellas' profile in the field of oncology**
- **Communicate Astellas' strategy and oncology pipeline to key target customers**
- **Communicate Xtandi and tivozanib data and common set of messages to EU affiliates' key target customers**
- **Gain an increased understanding of the current landscape in RCC and prostate cancer & the challenges Astellas will face when launching Xtandi and tivozanib in the EU**

**Target audience for meeting**

- **Mid – top level product OLs – those with the potential to be local product champions within the relevant EU markets**
- **Data – naïve customers, ie those who have not been involved in any APEL or national/local advisory board meetings prior to the pan EU ad board meeting**
- **10 per affiliate: 5 prostate/Xtandi and 5 RCC/ tivozanib***

***Turkey – 10CRPC OLs.'**

**The emails sent to the UK affiliate which reflected the selection criteria set out above, the email which the UK senior employee forwarded to UK managers, and the responses from this team compounded the unacceptability of the arrangements. In that regard the Panel noted the email from one of Astellas UK staff identifying health professionals who met these unacceptable criteria included '[city] is one of … main key accounts', '…one of our high users and would respond well to such a meeting…', '… is influential at a [city] level and more and more nationally with time' and 'This is a business move … barely sees industry, not using prechemo abi and once using he rarely changes'. The reserve nominations included '… I believe he has the reputation with us for being an abi man, however, this would give us the opportunity to convert him to the new way and '…is on our list and is influential, and would be good to engage at this level'.**

**The Panel did not accept Astellas Europe's submission in the case now under consideration that its provision of an incomplete and in the Panel's view misleading response was unintentional given Astellas' decision not to include the unapproved criteria following the dispatch of what Astellas described as a revised corrective email (December 2013). The Panel noted Astellas Europe's submission that it did not include the initial unapproved criteria in its response to Case AUTH/2747/1/15 as these were not the ultimate final criteria communicated to affiliates. It further noted the company's submission that there was no consideration at all as to whether the emails of 5 September and 17 October should be submitted as part of its response to the previous case, Case AUTH/2747/1/15. Astellas Europe acknowledged that its investigation into that complaint was inadequate.**

**The Panel was extremely concerned that Astellas Europe appeared to consider that ultimate revised final selection criteria had been communicated. In the Panel's view that was not so. Neither of the two emails dated 12 December sent from Astellas Europe contained revised selection criteria. The Panel noted Astellas Europe's submission that the teleconference held on 12 December discussed the revised selection criteria for attendees. In the Panel's view this should have been made abundantly clear in the emails of 12 December. Astellas Europe had not provided detailed information regarding the discussion on the teleconference. Given its comments above the Panel was not at all surprised by Astellas Europe's submission that none of its affiliates had subsequently requested any changes to those nominated as attendees. It was hard to understand why such a fundamental change to the selection criteria had not been made clear at the outset in either of the emails.**

**The Panel noted that the original selection criteria as set out in the three emails and the presentation to the Oncology Steering Committee dated 5 February 2013 were directly relevant to the subject matter of the complaint in Case AUTH/2747/1/15. In the Panel's view Astellas Europe had therefore provided not only an incomplete response to that complaint but also a misleading one.**

**The Panel noted Astellas Europe's submission that the final certification did not take place until the day before the meeting took place (26 February 2014) after health professionals had been selected and invitations sent.**

**In addition to the provision of an incomplete response, the Panel noted Astellas Europe's submission that it was now apparent that its representatives had misled the Appeal Board when the report was considered as the UK sales force had been involved in the nomination process.**

**The Panel noted Astellas Europe's submission that concerns had been raised in November 2013 and that in January 2014 it had received an anonymous complaint about the meeting which had been dealt with by the issuing of the revised selection criteria and thus no further action was taken. The Panel noted its comments above about the revised selection criteria and their communication. The Panel also noted that Astellas Europe's response to the Panel's request for further information was different to its initial submission in relation to whether the company knew about the emails and the changes to the selection criteria for attendees and had decided not to provide them or whether the company had not asked staff for materials etc other than those in the Zinc system. In the Panel's view Astellas had either not paid sufficient attention to ensuring that all relevant information had been supplied in its response to Case AUTH/2747/1/15 or had made a conscious decision to omit relevant details from that response. The Panel noted Astellas Europe's most recent submission in this regard that it had not considered the material at all.**

**The Panel was extremely concerned and disappointed by the conduct of Astellas Europe and Astellas UK. The integrity of self-regulation**

**relied upon the provision of complete and accurate information by pharmaceutical companies. The Panel considered that the failure to provide all the information and the misleading nature of what was submitted in Case AUTH/2747/1/15 meant that high standards had not been maintained. A breach was ruled as acknowledged by Astellas Europe. The circumstances brought discredit upon and reduced confidence in the pharmaceutical industry. The Panel ruled a breach of Clause 2 as acknowledged by Astellas Europe.**

**In relation to the allegations about the discussion of the case by a very senior employee of Astellas Europe, the Panel noted the comments made by staff interviewed about meetings which this individual had attended. It appeared that these were not 'Astellas town hall' meetings as stated by the complainant. It was not clear what the meeting referred to by the complainant was but the complaint was clear it was a meeting where this individual discussed the matter. The Panel was concerned that the interview guide for discussion with employees appeared to be biased and designed to encourage staff to confirm that they were impressed by the training and the 'Tone from the top'. Bearing in mind the difficulties for staff in being critical of senior management, the Panel was very concerned that a very senior employee of Astellas Europe's comments on the outcome of Case AUTH/2747/1/15 were viewed as dismissive and/ or that the matter was not taken seriously enough. This was compounded by the serious nature of that case. The details set out in the collated interview feedback master document appeared to be different to those provided elsewhere in the company's response. Nonetheless it was clear that despite the content and tone of the interview guide, certain staff were concerned about the impression given. The Panel was also concerned that staff recalled the phrases 'we were trying something different' and 'there are large grey areas in application of the code'. The Panel disagreed with the latter comment in relation to Case AUTH/2747/1/15 as the requirements for advisory boards and other such meetings were clear in the Code, supplementary information and guidance issued by the PMCPA.**

**The Panel considered, given the seriousness of Case AUTH/2747/1/15, it was completely unacceptable in the companies' discussion of that case for a very senior employee of Astellas Europe to give any impression that he and/or the company was dismissive of the Panel's rulings and the Appeal Board's consideration of the report from the Panel. The Panel considered that in this regard high standards had not been maintained and ruled a breach. In addition the Panel considered that the circumstances brought discredit upon and reduced confidence in the pharmaceutical industry. The Panel ruled a breach of Clause 2. These rulings were upheld on appeal by Astellas Europe.**

**The Panel considered that the circumstances regarding the failure to provide comprehensive, accurate information, the misleading nature of the submissions in Case AUTH/2747/1/15, the relevance of the omitted material and the discussion of the outcome of the case by Astellas Europe raised serious concerns about the companies' procedures. In this regard the Panel noted Astellas Europe's submission about its certification of the arrangements the day before the meeting in question. It also noted the Appeal Board's comments when considering the report from the Panel in Case AUTH/2747/1/15 that the company's standard operating procedures were either unclear or not followed and its questions over the rigour of Astellas Europe's certification process. This case also raised fundamental concerns regarding Astellas Europe and Astellas UK's approach to compliance and self-regulation.**

**The Panel noted its comments above regarding the position of Astellas UK and Astellas Europe in relation to this case. The Panel considered that its serious concerns warranted reporting Astellas Europe and Astellas UK to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure.**

**In relation to the report from the Panel, Astellas Europe contacted the PMCPA in September to advise that it had recently discovered information which the company wished to provide to the Appeal Board in relation to its consideration of the report from the Panel. The Chairman of the Appeal Board agreed that Astellas Pharma Europe could submit further information in relation to the report. The information did not relate to Astellas UK.**

**Astellas Europe stated that it had conducted a number of staff interviews as part of its continued human resources investigation and an email had been discovered which it considered to be the source of the concerns that were raised in November 2013 about the advisory board at issue in Case AUTH/2747/1/15.**

**The email, from a senior employee at Astellas Europe was dated 26 October 2013 and indicated that the sender was instructing the team to remove an unacceptable objective for the advisory board from the meeting agenda in order to 'smooth the passage' of the meeting through the approval process, but unfortunately made it clear that this was still a key objective of the advisory board.**

**Astellas Europe referred to the background and submitted that the email indicated that there was a conscious decision by one individual to circumvent the established approval process in order to incorporate an unacceptable objective in to an advisory board.**

**Astellas Europe submitted that the email appeared to be the trigger for the activities that took place in late 2013 to reassess the meeting and address the concerns raised. Two of the four members of staff in receipt of the email of 26 October 2013, whilst not sharing or discussing the email directly with anyone, raised their concerns about the meeting. The activities in November and December 2013 were as a consequence of this in an attempt to correct the issues raised eg the teleconference and emails of 12 December 2013.**

**Astellas Europe as an organisation stated that it was not aware of the emails until 22 September 2015 which was why they were not submitted in the company's response to Case AUTH/2780/7/15. This was particularly disappointing, given that the individual in question was asked for all relevant information.**

**At the consideration of the report Astellas Europe and Astellas UK stated that the companies recognised that the investigation and response to Case AUTH/2747/1/15 was inadequate. The companies submitted that there was no dishonesty or deliberate attempt to mislead. The investigation had identified that an individual senior member of staff central to this situation withheld key information from Astellas Europe, the Panel and Appeal Board. Immediate action had been taken to address the conduct of this senior member of staff. Astellas incorrectly assumed that there was no sales involvement in nominating UK health professionals to attend the advisory board and therefore it unintentionally provided inaccurate information to the Appeal Board.**

**Astellas accepted the Panel's rulings of breaches of the Code and deeply regretted that it had brought disrepute on the pharmaceutical industry.**

**Astellas Europe stated that it had already undertaken a number of measures and gave details of its key compliance activities since the completion of Case AUTH/2747/1/15. Details were provided.**

**The Appeal Board noted the Panel's comments and rulings including its ruling of a breach of Clause 2 and the outcome of the appeal where the Appeal Board upheld a second Panel ruling of a breach of Clause 2. The Appeal Board was extremely concerned about the approach to compliance and poor communication across Astellas Europe and Astellas UK.**

**The Appeal Board noted the Panel's comments that the original selection criteria for Astellas Europe's Pan-European Uro-oncology Advisory Board Meeting were directly relevant to the subject matter of the complaint in Case AUTH/2747/1/15 yet these had not been provided by the company in its response to that case.**

**The Appeal Board was also very concerned about why the email dated 26 October 2013, sent by the senior employee of Astellas Europe was not previously provided. The Appeal Board noted from Astellas that two recipients of the email had raised concerns about the meeting back in 2013 but they had not disclosed the email itself. Astellas stated that the email was handed to senior management on 22 September 2015. The Appeal Board was concerned that such relevant information had not surfaced until this late stage.**

**The Appeal Board was very concerned about the culture of the organisations and that despite a prior internal complaint raising the issue it had taken two complaints under the Code and a late submission of evidence in the present case to produce comprehensive information concerning selection of the delegates for the meeting at issue.**

**The Appeal Board was concerned that the arrangements had been reviewed and approved by the UK affiliate. Astellas Europe certified the arrangements the day before the advisory board at issue took place.**

**The Appeal Board considered that Astellas had provided not only an incomplete response to the original complaint but also a misleading one. The Appeal Board considered that self-regulation relied upon the provision of complete and accurate information by pharmaceutical companies. Astellas's omission was totally unacceptable. The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure that both Astellas Europe and Astellas UK should be publicly reprimanded for this failure.**

**The Appeal Board noted that the UK health professionals who attended the meeting had been provided with a corrective statement and a case report which was misleading. This was totally unacceptable. Consequently the Appeal Board decided, in accordance with Paragraph 11.3 of the Constitution and Procedure, to require Astellas Europe and Astellas UK to issue a corrective statement to all the UK attendees at the meeting to clarify the position. The corrective statement should refer to both case reports. Under Paragraph 11.3 details of the proposed content and mode and timing of dissemination of the corrective statement must be provided to the Appeal Board for approval prior to use. [The corrective statement appears at the end of the report.]**

**The Appeal Board also decided that, given all of its concerns about the conduct of Astellas as set out above, to require, in accordance with Paragraph 11.3 of the Constitution and Procedure, an audit of both Astellas Europe and Astellas UK's procedures in relation to the Code. The audit would take place in December 2015. On receipt of the audit report, the Appeal Board would consider whether further sanctions were necessary including the possibility of reporting the companies to the ABPI Board of Management (Paragraph 12 of the Constitution and Procedure).**

**Astellas Pharma Europe and Astellas UK were each audited in December 2015 and on receipt of the report of the audits, the Appeal Board was extremely concerned that despite a very critical report that highlighted numerous serious concerns including the companies' cultures and a reference to Astellas Europe's institutional failure with respect to compliance, neither Astellas Europe nor Astellas UK provided any detail on when and how each would address those concerns.**

**The Appeal Board decided that both companies should be re-audited but it deferred setting a date for such until each had provided a detailed compliance action plan and comprehensive response to the recommendations in the report of the audits. The Appeal Board discussed further sanctions including, again, whether there should be a report to the ABPI Board. The Appeal Board concluded that on receipt of the report for the re-audits it would decide whether further sanctions were necessary.**

**The companies subsequently provided a further detailed response as requested. The Appeal Board noted that the companies would need time for their stated compliance objectives to be completed or get underway. In that regard the Appeal Board decided that Astellas Pharma Europe and Astellas UK should each be re-audited in September 2016 by which time both would be expected to demonstrate significant improvement.**

**During the Code of Practice Appeal Board's consideration of the audit reports for Astellas Europe and Astellas UK (25 February 2016) it noted a letter from Astellas Europe (17 February) which stated that new information had been discovered as a result of further investigation which would assist the understanding of the full circumstances of these cases and this would be sent to the PMCPA. On receipt of further information from Astellas Europe the original Panel was reconvened to consider the matter.**

**The detailed response from Astellas Europe is given below and included a report by external counsel which was asked by Astellas Pharma Inc to conduct an investigation.**

**The Panel noted the circumstances surrounding Cases AUTH/2747/1/15 and AUTH/2780/7/15, the reports to the Appeal Board, the findings of the audits, particularly those relevant to Astellas Europe, and the additional information now provided by Astellas Europe. The companies were to be re-audited in September 2016.**

**The Panel noted that the additional information was provided by, and concerned acts and omissions by, Astellas Europe. The Panel noted that Astellas Europe was not a member of the ABPI, although it was a member of EFPIA. Astellas UK was a member of the ABPI. The Panel had previously noted that Astellas UK was responsible for the acts/omissions of its affiliates that fell within the scope of the Code including its UK based European headquarters. In the present matter, the Panel noted that the position of Astellas UK remained as set out above.**

**The Panel noted all the concerns and comments it had raised previously. It was appalled at the conduct of senior managers as revealed in the additional information in relation to the two cases and resulting audits. Senior managers failed to provide full and accurate details to the Panel, the Appeal Board and the Authority in relation to the audits. Some very important details, although hinted at by the Panel, the Appeal Board and by the Authority in the report of the audits, had only come properly to light as a result of the follow-up investigation ordered by Astellas Japan and carried out by an external counsel. This might, in part, have been triggered by the audits including the conversation the PMCPA had with the CEO and President Astellas Group.**

**The report from external counsel stated that all those involved in compiling the information and drafting the response to Case AUTH/2747/1/15 were aware of the existence of the original selection criteria, as on 30 January 2015 senior employees' attention was drawn to the email which set out the original selection criteria. This was inconsistent with Astellas Europe's original response.**

**The report from external counsel noted that the company's investigation following receipt of the second complaint (Case AUTH/2780/7/15) was inadequate. The external counsel report noted that the failure to conduct a thorough fact-finding exercise at any time following the first PMCPA complaint was concerning and was even more troubling given the number of senior staff who knew exactly where to look for the relevant material. Further details about the content of the report from the external counsel appear below.**

**The Panel considered that the additional information demonstrated that a number of individuals in Astellas Europe had not provided complete and accurate information. That this included very senior employees was extremely concerning. Astellas Europe's conduct was completely unacceptable. The report of the audits had found that there was an institutional failure with respect to compliance; a finding which, in the Panel's view, was now compounded by the additional information including the report by external counsel. The failings of Astellas Europe, as demonstrated by the additional information, went beyond, and were arguably even more serious than, those outlined in the report of the audits. The latest information demonstrated that Astellas Europe staff had lied about the original selection criteria on a number of occasions and not limited to Astellas Europe's response to the complaints but including when interviewed individually by members of the Authority at the audit, when they appeared before the Appeal Board in relation to the reports from the Panel in both cases and at the appeal in Case AUTH/2780/7/15. The failure to provide accurate, complete information at an audit and to the Appeal Board was a very serious matter. The truthfulness and accuracy of such comments and submissions to the Authority was fundamental to the integrity of self-regulation. It was remarkable that the individuals concerned had not provided the correct information sooner despite having had every opportunity to do so; the true position only emerged after those from the PMCPA carrying out the audits had spoken to the Japanese parent company and a report from external counsel was commissioned. The Panel was also concerned about the newly revealed breadth of compliance failures such as flawed processes including human resources processes wherein vital compliance material was not recognized as such, and the apparently unfettered influence of the named senior individuals upon matters such as disciplinary investigations. The Panel noted that very senior employees had left Astellas Europe. The Panel decided that it would report Astellas Europe to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to consider in relation to Paragraphs 11.3 and 11.4 of the Constitution and Procedure. Astellas UK would be advised accordingly.**

**The detailed comments from Astellas Europe and Astellas UK on the report from the Panel appear below.**

**In summary the representatives from Astellas Europe sincerely apologised for the significant cultural and compliance failings created and caused by the actions and behaviours of some of its very senior managers. Globally Astellas viewed the current position as a corporate crisis. The newly appointed President of Astellas Europe stressed his commitment to improve corporate culture such that ethics and compliance were embedded throughout the organisation. Some of that cultural change would come through the appointment of new people into key roles.**

**The UK company was committed to working closer with Astellas Europe to clarify responsibilities and to ensure that the UK approved and certified any activity undertaken by its European affiliates that involved a UK health professional or took place in the UK. The company would also take responsibility for any future complaints under the Code about such activities.**

**The Appeal Board welcomed the full apology made by the representatives of Astellas Europe at the consideration of the report, particularly as no apology was included in the papers for the case. However, the Appeal Board considered that such multiple organisational and cultural failings meant that this was one of the worst cases it had ever had to consider. There was an institutional failure with respect to compliance. Very senior staff had lied and there was deception on a grand scale. The Appeal Board was appalled and astonished that senior managers from Astellas Europe had made a concerted attempt to deceive it and the PMCPA. In that regard the Appeal Board considered the PMCPA's foresight to interview the Global CEO and President of Astellas Inc during the audit was pivotal in bringing these failings to light. It was a truly shocking state of affairs. The Appeal Board noted that these concerns did not relate to Astellas UK.**

**This was the third time Astellas Europe had been reported to the Appeal Board by the Panel and the second time Astellas UK had been reported to the Appeal Board by the Panel (including Case AUTH/2747/1/15).**

**The Appeal Board whilst recognising the difficulties of the situation, considered that Astellas UK should have attempted to exercise greater control on compliance matters in relation to the meeting at issue, the investigation of and response to the complaints and the Panel's reports to the Appeal Board. This was especially important given that Astellas UK was responsible for the acts/omission of its affiliates that fell within the scope of the Code including its UK based European headquarters. Given the information about the lies and deception, it was not surprising that Astellas Europe had asserted itself and taken the lead in responding to Cases AUTH/2747/1/15 and AUTH/2780/7/15.**

**The Appeal Board noted that Astellas Europe, as a member of EFPIA, was bound by the codes of EFPIA member associations including any applicable sanctions.**

**The Appeal Board considered that the integrity of self-regulation was reliant upon pharmaceutical companies providing complete and accurate information. The conduct of senior staff at Astellas Europe had been totally unacceptable and potentially harmful to self-regulation in this regard. It was also disappointing that Astellas UK had not taken firm action. There were multiple failings in these cases. The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure that both Astellas Europe and Astellas UK should again be publicly reprimanded for this failure.**

**The Appeal Board noted that the UK health professionals who attended the meeting had been provided with two corrective statements and case reports which, given the emergence of new information, gave a misleading account of the arrangements for the meeting at issue. This was wholly unacceptable. Consequently the Appeal Board decided, in accordance with Paragraph 11.3 of the Constitution and Procedure, to require Astellas Europe and Astellas UK to issue a fresh corrective statement to all the UK attendees at the meeting to clarify the position. This would be the third corrective statement. [The corrective statement appears at the end of the report.]**

**The Appeal Board also decided, given the seriousness of the failings, its concerns about the conduct of Astellas as set out above and the responsibility of Astellas UK for its parent company, to report Astellas Europe and Astellas UK to the ABPI Board of Management. This was in accordance with Paragraph 12.1 of the Constitution and Procedure.**

**The ABPI Board noted that breaches of the Code had been ruled including Clause 2. The companies had been reported to the Appeal Board and both had been publicly reprimanded and required to issue corrective statements. The companies had been audited in December 2015 and were to be re-audited in September 2016.**

**The ABPI Board was extremely concerned at the multiple organisational and cultural failings at Astellas. There was an institutional failure. Very senior staff at Astellas Europe had lied and there was deception on a grand scale which was appalling and shocking.**

**The totally unacceptable behaviour of senior staff at Astellas Europe was potentially harmful to the integrity of self-regulation which relied upon companies providing complete and accurate information. The ABPI Board noted that Astellas UK was the member of the ABPI and that Astellas UK was responsible for the acts/omissions of affiliates that fell within the scope of the Code including its UK based European headquarters.**

**The ABPI Board decided that Astellas UK should be suspended from membership of the ABPI for a period of 12 months commencing 24 June. The ABPI Board also decided that it wanted sight of the reports of the September 2016 re-audits of Astellas UK and**

**Astellas Europe so that it could review the position, including the length of the suspension, before the end of 2016. The re-audits must show demonstrable improvements at both companies particularly in relation to corporate culture.**

**Astellas UK and Astellas Europe were re-audited in September 2016 and the report of the audits was considered by the Appeal Board in November.**

**The Appeal Board noted that although both companies had worked hard to implement the recommendations from the previous audits and to ensure compliance was truly embedded, there was still work to do.**

**With regard to Astellas Europe, the Appeal Board noted that the institutional failure with respect to compliance was starting to change. Both companies had, *inter alia*, issues with certification. The Appeal Board decided that both should be re-audited in April 2017 and on receipt of the report for those re-audits it would decide whether further sanctions were necessary.**

**At its meeting in December, the ABPI Board reviewed the progress made by both companies and the work still to be completed noting that it took time to change culture and to truly embed compliance. It noted the Appeal Board's decision that both companies should be re-audited in April 2017. Although the ABPI Board was encouraged by the improvements and progress made by both Astellas Europe and Astellas UK it decided that the suspension of Astellas UK from membership of the ABPI should continue. The ABPI Board would review the position in June after the re-audits.**

**Astellas UK and Astellas Europe were re-audited in April 2017 and the report of the audits was considered by the Appeal Board in May 2017.**

**The Appeal Board noted that Astellas UK and Astellas Europe were now working more closely and there was more open communication with staff. Both companies had been working to implement the recommendations of the previous audits and to ensure compliance was embedded. However, the Appeal Board noted the number of issues highlighted in the report and that there was still much work to be done.**

**The Appeal Board accepted that it took a long time to change culture but it was not convinced that progress was being made at an appropriate speed particularly given the issues that had come to light in Cases AUTH/2883/10/16, AUTH/2939/2/17 and AUTH/2940/2/17. This was particularly worrying given the level of scrutiny the companies were under. In the view of the Appeal Board, Astellas had much work still to do.**

**In relation to Case AUTH/2780/7/15 the Appeal Board decided that both companies should be re-audited in October 2017 at the same time as the audits required in Cases AUTH/2939/2/17 and AUTH/2940/2/17 and the re-audit in Case AUTH/2883/10/16 (Astellas UK only).**

**The Appeal Board noted the outcome of the audit in Case AUTH/2883/10/16 and the re-audits in Case AUTH/2780/7/15, the decisions to report Astellas UK to the ABPI Board in relation to Case AUTH/2883/10/16 and Astellas UK and Astellas Europe in relation to Cases AUTH/2939/2/17 and AUTH/2940/2/17. It also noted its concerns regarding the lamentable lack of concern for patient safety and wholly inadequate oversight and control. Whilst noting this was a matter for the ABPI Board, the Appeal Board's view was that Astellas UK was not ready to resume membership of the ABPI and the suspension should continue.**

**At its meeting in June 2017 the ABPI Board agreed with the Appeal Board's comments and concerns about the re-audits in April 2017.**

**The ABPI Board noted and endorsed the Appeal Board's views about the total failure of the companies' systems in relation to the control of prescribing information, the lamentable lack of concern for patient safety, wholly inadequate oversight and control and initial lack of urgency. It was a woeful state of affairs.**

**The ABPI Board gave serious consideration to expelling Astellas UK from membership of the ABPI. However, it noted the commitments from Astellas Europe, the global company and of the new UK General Manager. The companies had made voluntary admissions and it was now imperative that the October re-audits showed significant progress.**

**The ABPI Board decided that it would extend the suspension of Astellas UK from membership of the ABPI for another 12 months. This further period would run uninterruptedly from the initial period of suspension and would then amount to the maximum suspension (two years) allowed under the ABPI Articles of Association.**

**The ABPI Board also decided that it wanted sight of the report of the October 2017 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of 2017. If the report of the re-audits did not show significant improvement and progress at both companies, then the ABPI Board would consider expelling Astellas UK from membership of the ABPI. The companies should consider undergoing an external assessment of progress, particularly in relation to risk management of compliance in the broadest sense, ie including matters beyond the scope of the Code, with the outcome to be available at the time of the October 2017 re-audits.**

**The ABPI Board also decided that the MHRA should be advised of the ABPI Board's very serious concerns about the conduct of Astellas UK and Astellas Europe particularly in relation to the matters concerning patient safety. EFPIA should also be updated and asked to ensure the EFPIA Board was informed of the position.**

**Astellas UK and Astellas Europe were re-audited in October 2017 and the report of the re-audit**

**was considered in November. The Appeal Board noted that as these were the fourth audits of the companies and given that Astellas UK was currently suspended from membership of the ABPI, it expected substantial progress and improvements from both companies. This expectation had not been met. The Appeal Board acknowledged that some progress had been made. The companies must take prompt action to implement the findings and recommendations in the report of the October 2017 re-audits.**

**The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been positive changes in the company culture. However, it was not convinced that the expected progress was being made, especially since the April 2017 re-audits. Overall, the Appeal Board's view was that the rate of progress was inadequate and that the companies were not where they should be. There was still much work to do. The Appeal Board queried whether there was an element of structural inertia or perhaps fear of wrongdoing which was inhibiting or slowing the rate of progress.**

**Despite its criticisms, the Appeal Board noted the positive steps taken by the leadership of Astellas to engage more broadly with staff and drive changes.**

**The Appeal Board decided that both companies should be re-audited in April 2018. At which point it expected the 2018 global staff survey to demonstrate improvements at Astellas Europe and Astellas UK.**

**Whilst noting that this was entirely a matter for the ABPI Board, the Appeal Board's view was that if the report of the October 2017 re-audits and Astellas' response had come at the end of the two year suspension limit, then Astellas would have fallen well short of the standard required to resume membership of the ABPI. Unless substantial progress was seen in the report of the re-audits in April 2018, in the Appeal Board's view, Astellas UK would be at serious risk of a recommendation that it be expelled from membership of the ABPI.**

**The ABPI Board noted the Appeal Board's comments and concerns about the re-audits in October 2017 and the additional information provided by Astellas.**

**With regard to the external assessment of progress, particularly in relation to risk management of compliance in the broadest sense ie including matters beyond the scope of the Code, the ABPI Board noted the information provided by Astellas.**

**Following a change in tone from the top of Astellas, the ABPI Board recognised that meaningful progress had been made by the companies. The ABPI Board understood the difficulty inherent in making wide-sweeping cultural changes, and how long it took for those changes to become fully embedded within a large organisation. However, the ABPI Board acknowledged Astellas' clear commitment to further improvement.**

**The ABPI Board noted Astellas' statement that its materials were compliant in May 2017 in relation to issues of patient safety.**

**The ABPI Board also decided that it wanted sight of the report of the April 2018 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of the current suspension in June 2018.**

**The ABPI Board decided that taking all the circumstances into account it would take no further action at this stage in relation to the expulsion of Astellas from membership of the ABPI. The suspension from membership of the ABPI would remain in place until June 2018.**

**The ABPI Board also decided that the MHRA should be advised of the position. EFPIA should also be updated and asked to ensure that the EFPIA Board was informed of the position.**

**Astellas UK and Astellas Europe were re-audited in April 2018 and the report of the re-audits was considered in May 2018.**

**The Appeal Board noted the detailed responses from Astellas to the report of the April 2018 re-audits including that it was an accurate reflection of the work undertaken.**

**The Appeal Board noted the results of the 2018 staff survey and the progress made. Numerical increases had been shown in a number of parameters since the previous survey in July 2017. There were concerns about the comments made by staff. The Appeal Board also noted the differences in the Astellas UK results which were generally better than the Astellas Europe results. The Appeal Board considered that the Astellas Europe management committee scores although improved were still not where they should be.**

**The Appeal Board noted the comments in the report of the April 2018 re-audits and considered that both the leadership of Astellas Europe and Astellas UK had engaged with staff to bring about progress. There was still work to be done. The Appeal Board noted one of the recommendations was that members of the leadership team at Astellas Europe should be held to account and be challenged on compliance matters.**

**The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been further positive changes in the company culture and this needed to be continued. The Appeal Board noted that there had been some positive compliance initiatives. The discussion fora and communications continued and progress had been made including ensuring staff had time to complete training.**

**The Appeal Board noted that whilst as a percentage there had been a significant increase in the number of job bags, the overall number was still low. As Astellas increased its activities it must remain**

**extremely vigilant to compliance requirements in particular in relation to certain higher risk activities such as patient support programmes, product launches etc. The true test of the compliance framework in Astellas and its approach would be when activity levels including higher risk activities were increased and the company was operating at business as usual.**

**The Appeal Board considered that, at long last, the re-audits in April 2018 showed that progress had been made and that the companies were building on momentum started in summer 2017. The Appeal Board was concerned that these were the fifth audits of each company and that the first audits were in December 2015. It was extraordinary that it had taken so long to demonstrate meaningful change. The overall impression from the report of the April 2018 re-audits was that Astellas was showing improvement and momentum. However, whilst the companies had reached a certain level, given all the circumstances including that Astellas UK had been suspended from membership of the ABPI and that the Appeal Board still had concerns, the Appeal Board decided that Astellas Europe and Astellas UK should each be re-audited at the end of the first quarter of 2019 to ensure that the improvements and the momentum continued and were built upon.**

**On the information before it, and noting that Astellas UK was still to respond to the PMCPA in relation to matters raised following completion of the consideration of a complaint concerning Astellas UK, Case AUTH/2984/10/17, the Appeal Board decided that sufficient progress had been made by the companies such that the Appeal Board did not consider that it warranted a recommendation for the expulsion of Astellas UK from membership of the ABPI when the matter came before the ABPI Board on 5 June 2018.**

**In June 2018 the ABPI Board noted the comments from both the Appeal Board and Astellas.**

**The ABPI Board noted the limited information provided about matters raised in Case AUTH/2984/10/17. This was still to be considered by the PMCPA and the Appeal Board and was not before the ABPI Board for consideration.**

**The view of the Appeal Board was clear. The ABPI Board agreed with the Appeal Board's views and assessment of the re-audits and concluded that meaningful progress had now been made.**

**The ABPI Board believed that the culture in the companies had improved and noted that much of this had been led by the General Manager of Astellas UK. However, the Board recognised the importance of an ongoing commitment to ensure sustained culture change. On reviewing all the material, the ABPI Board had concerns about the sustainability of the changes made given that there had already been five audits/re-audits, and especially as further types of activity were still to be fully re-introduced across the companies.**

**The ABPI Board therefore decided that it wanted to see the report of the 2019 re-audits and be informed of major developments including the outcome of Case AUTH/2984/10/17.**

**In the circumstances, there was no need for the ABPI Board to consider expelling Astellas UK from membership of the ABPI. The suspension would end on 24 June 2018 and Astellas would revert to full membership of the ABPI.**
**The ABPI Board also decided that the MHRA should be advised of the position and that EFPIA should be updated and asked to ensure that the EFPIA Board was informed of the position.**

**Astellas UK and Astellas Europe were re-audited in April 2019 and the report of the re-audits was considered in May 2019.**

**The Appeal Board noted the detailed response from Astellas Europe and Astellas UK to the report of the April 2019 re-audits.**

**The Appeal Board noted two new senior appointments; a new President EMEA Operations who joined Astellas in July 2018 and a new General Manager, Astellas UK who was appointed from April 2019.**

**The Appeal Board noted from the report of the April 2019 re-audits that it appeared that a more compliant culture was embedded within Astellas with improved communication. It was essential that this was maintained.**

**The Appeal Board considered that Astellas UK must ensure a proper professional approach to investigating and responding to any complaint under the Code such that the shortcomings in Case AUTH/2984/10/17 were not repeated. The Appeal Board noted that an audit had not been required in Case AUTH/2984/10/17. The case had, in accordance with established practice, been discussed as part of an examination of the company's culture at the re-audits.**

**The Appeal Board noted that these were the sixth audits/re-audits of each company and that the first audits were in December 2015. The Appeal Board considered that, on the information provided in the report of the April 2019 re-audits, it appeared that the companies had made further improvements, that this would be maintained and broadly the companies were where they should be. The Appeal Board, however, remained very concerned about the amount of time it had taken Astellas to reach this point. The Appeal Board noted that Astellas stated that it would follow up on the issues identified in the report of the April 2019 re-audits and it was committed to maintaining its approach to embedding a sustainable compliance culture. The Appeal Board noted a number of activities/actions were due to be undertaken. On the understanding that this work was completed, that the progress shown to date was continued and a company-wide commitment to compliance was maintained, the Appeal Board decided that, on the basis of the information in the report of April 2019 re-audits, no further action was required in relation to Case AUTH/2780/7/15, Case AUTH/2883/10/16, Cases AUTH/2939/2/17 and AUTH/2940/2/17.**

**The Appeal Board noted that the audit/re-audits in these four cases had been required by the Appeal Board. They had not been required by the ABPI Board. Nonetheless, the Appeal Board noted the ABPI Board's request to see the report of the April 2019 re-audits.**

**At the re-audits in April 2019 it was noted that the MHRA decided that Astellas advertising materials should be submitted for review. This was introduced for all new materials issued since 1 December 2018.**

**In June 2019 the ABPI Board received an update as requested. It noted the comments from both the Appeal Board and Astellas and the improvements made.**

An anonymous and non-contactable complainant who appeared to be an employee of Astellas complained about the truthfulness of Astellas's response to Case AUTH/2747/1/15. Case AUTH/2747/1/15 concerned the arrangements for a meeting organised by Astellas Pharma Europe and held in Milan in February 2014. In that case the company was ruled in breach of the Code including Clause 2 and was required by the Appeal Board to issue a corrective statement to all UK attendees.

The complainant provided an email dated 5 September 2013 from an agency to an employee at the Astellas Turkey affiliate and copied to a senior employee at Astellas Europe and six others. It was headed 'email from [named employee]; 3rd Pan EU Expert meeting in February 2014'. This email referred to one attachment which was described as a 'top-line guide to the meeting' which outlined the proposed process for the meeting. The email stated that it was asking each affiliate to provide details of 30 opinion leaders in priority order who should be mid to top level opinion leaders with the potential to be local product champions within the relevant market and data naïve customers ie those who had not been involved in Astellas Europe national/local advisory board meetings. There was also a request for an Astellas affiliate contact who could be approached concerning delegate nominations. The complainant did not provide a copy of the attachment.

**COMPLAINT**

The complainant stated that Astellas legal and compliance colleagues recently provided training on the outcome of Case AUTH/2747/1/15 and its learnings. In addition, a 'town hall' meeting was convened, where a very senior employee of Astellas Europe discussed the matter, albeit in a very dismissive manner.

The complainant stated that it was extremely alarming and concerning that the account given to the PMCPA in the response by Astellas was knowingly false and intentionally misleading. In its response to Case AUTH/2747/1/15 Astellas claimed that all invitees and participants were identified and grouped based on their 'clinical expertise' and 'experience of treating patients with mCRPC' (metastatic castration – resistant prostate cancer). Unfortunately, nothing was further from the truth and Astellas knew that but deliberately chose to conceal it from the PMCPA. The complainant provided a copy of the briefing given by Astellas to its affiliates in which it was clearly stated that all 30 opinion leaders chosen by each affiliate had to be; 'mid to top level opinion leaders with the potential to be local product champions'. Furthermore it was requested that they be 'data naïve'. The complainant alleged that this directly contradicted the claim made that they were chosen based on their clinical expertise.

The complainant stated that it was also disappointing that Astellas had still not learnt from the rulings of breaches of the Code including Clause 2, and that the company had deliberately misled the PMCPA about a very serious complaint. The complainant urged the Authority to consider more serious sanctions and submitted that given the gravity and seriousness of this very deliberate lie, consideration should be given to an immediate audit of the company's procedures, a public reprimand and possible suspension or exclusion from membership of the ABPI.

When writing to Astellas Europe attention was drawn to Clauses 2 and 9.1.

**RESPONSE**

Astellas Europe stated that it was disappointed to receive the complaint, as the company had measures in place, including an ethics help line, to facilitate the anonymous reporting of employee concerns and encouraged employees to raise such concerns. Astellas Europe supported employees who raised concerns and the company was committed to addressing anything which was not aligned with the requirements of the Code.

The email provided by the complainant dated 5 September 2013 was sent on behalf of Astellas Europe by the agency co-ordinating the organisation of the advisory board at issue in Case AUTH/2747/1/15 to the general manager of the Astellas affiliate in Turkey.

Before addressing the complaint, Astellas Europe provided background to the series of events leading up to the advisory board at issue in Case AUTH/2747/1/15. Some of the events had only become apparent to Astellas Europe during the investigation into this complaint (Case AUTH/2780/7/15).

**Chronology of key events**

**4 September 2013**

During Astellas Europe's investigation of the present complaint, and as background to the email, the company discovered that a draft of this email was sent on 4 September 2013 by the agency organising the advisory board on Astellas Europe's behalf, to a senior employee in oncology at Astellas Europe, with a suggested text for an email to affiliate general managers which 'provides an overview and outline of the proposed process for the meeting, along with

a request for the name of a contact in the affiliate who we can contact concerning nominations for the meeting'. This text was almost identical to that included in the email provided by the complainant and the selection criteria contained in both were based on those discussed in February 2013 at the Oncology Steering Committee (which consisted of representatives from Astellas affiliates in the Nordics, France, Germany, UK, Spain, Czech/Slovak, Italy and Poland). There was no record of Astellas Europe notifying the agency that the text was appropriate to send but the senior employee concerned recalled that he 'must have done'. A copy of the agency email and the presentation given at the Oncology Steering Committee in February 2013 were provided.

**5 September 2013**

Astellas Europe stated that the following day, 5 September 2013, a slightly amended version of the email was sent by the agency to the general managers, and in some cases the oncology business unit director (where this position existed) of the Astellas affiliates in Belgium, Hungary, Russia, South East Europe, Spain, France, Italy, Turkey and Portugal. The email, *inter alia*, noted that each Astellas affiliate was being asked to nominate health professionals to attend the advisory board and listed certain criteria for these potential attendees. Astellas Europe submitted that this appeared to be the email that the complainant provided.

**October 2013**

Astellas Europe stated that in October 2013 it was decided to expand the scope of the advisory board as it was considered important to gain advice from health professionals in countries that were likely to be an early launch market; the relevant countries were UK, Germany, the Nordics, South Africa and the Netherlands.

**9, 10 and 11 October 2013**

Astellas Europe stated that in October 2013 an email was sent to the UK affiliate asking for a key contact for the agency organising the meeting and inviting a member of the UK team to attend one of two teleconferences in relation to the meeting (to be held on 10 and 11 October 2013) 'to discuss the focus of the Feb meeting, and implications for the target audience at the meeting'. A member of the UK team was nominated, was sent and tentatively accepted an invitation to the teleconference on 11 October 2013. During the investigation of this complaint this member of the UK team confirmed that he attended the teleconference. A discussion was also held with the Astellas member of staff who ran this teleconference who confirmed that the criteria specified in the email of 5 September were not discussed. Reference to 'implications for the target audience at the meeting' was in relation to whether the attendees were oncologists, urologists and/or uro-oncologists.

**17 October 2013**

Astellas Europe stated that on 17 October 2013 an email was sent by the agency to a senior employee in Astellas UK reiterating the same criteria for selecting attendees that were in the email of 5 September. The email requested that the UK provide nominated health professionals by 23 October 2013.

Although not documented, Astellas Europe understood from Astellas UK that there were two main criteria used to select potential health professional participants:

- That they were either urologists (given that the anticipated change to the licence was going to bring enzalutamide in to an earlier timeframe for treatment, potentially one in which urologists would have a greater role)

- Or that they were oncologists who saw a high volume of patients in clinics and had very practical experience of treating patients that were chemo-naïve.

The reasoning behind these criteria were that enzalutamide, which had broadly similar efficacy data in comparison with the already licensed direct competitor but with some advantages in terms of dosing, administration, monitoring and quality of life, was expected to soon be licensed for chemotherapy-naïve patients. Astellas UK wanted to understand from clinicians with high clinical workloads if these factors would fundamentally change treatment paradigms, specifically around the lack of routine monitoring and the theoretical benefit of saving valuable clinic time. In theory there would be a significant advantage with enzalutamide but there were reports of many clinicians not observing the strict monitoring requirements of the competitor product. The UK needed to understand the 'real world' scenario.

**21 October 2013**

Astellas Europe stated that the investigation conducted in relation to this complaint highlighted that, unbeknown to, and without any briefing from, Astellas, this email was forwarded by the UK senior employee in its entirety on 21 October 2013 to a UK management team which consisted of the medical and commercial members noting that 'we need to get back with nominations of customers for this event'.

**22 and 23 October 2013**

The following day (22 October 2013) one of the commercial managers replied with a list of seven UK health professionals to be put forward in the nomination process. It could be seen from this email that wholly inappropriate language was used to describe these health professionals as potential advisory board participants eg '.....is one of the.... main key accounts'; '....is one of our high users'; ...

advocate…'; '…influential…'; '…this is a business move…'; '…barely sees industry…'. On 24 October 2013 another reply was received from another manager with a further 30 nominations.

**November 2013**

Astellas Europe stated that on 7 November 2013 a UK senior employee sent an email to the agency with the 39 finally nominated health professionals. On the same day the agency sent out 'save the date' cards. During the investigation of this complaint Astellas Europe asked the UK affiliate to confirm who had nominated the further two health professionals above those nominated by the UK managers but the UK had no record of this.

In November 2013, concerns were raised internally about the advisory board. Further discussions took place and a decision was taken to issue a corrective email to address the inappropriate criteria previously communicated to the affiliates and to change the working groups from international sessions to national working group sessions at the meeting.

**12 December 2013**

Astellas Europe stated that a teleconference was held on 12 December 2013 with affiliates involved in the advisory board to discuss a number of changes to the format and organisation of the meeting, one aspect being the revised selection criteria for attendees. Affiliates were asked, in the light of the revised selection criteria, to reassess whether the health professionals already nominated were appropriate. No affiliate changed the health professionals that they had nominated.

On the same day an email including revised selection criteria was sent to affiliates. Also a separate email was sent to affiliates asking whether they wanted to run their own workshop on the day of the advisory board meeting or run an Astellas developed workshop. This email also noted 'Please also let Astellas know by end of play on Monday the 16th December whether there are any issues from a national compliance perspective given the change from international working group sessions to national working group sessions at the meeting'; 'Please also discuss the meeting with your affiliate's compliance/zinc manager by the end of this week/ beginning of next week and answer any questions that they have to ensure that the meeting is rapidly reviewed as soon as the meeting approval form becomes available on the system once again'.

**17 December 2013**

Astellas Europe stated that on 17 December 2013 the UK senior employee confirmed that he had spoken to a senior Astellas UK medical employee who had given him 'enough comfort that this meeting was ok under the circumstances'. The discussion was in relation to the change from there being national rather than international workshops at the meeting. The UK senior employee confirmed the UK would be 'moving ahead and would appreciate starting with the Astellas structure for content and agenda but would chair and run ourselves'.

**30 December 2013**

Astellas Europe stated that on 30 December 2013 formal invitations were sent to potential attendees.

**January 2014**

Astellas Europe stated that in January 2014, an anonymous internal complaint was received which consisted of a copy of an email very similar to the one provided by the complainant in this case. No other documentation was received. Astellas Europe considered that it had dealt with this in the previous December by issuing the revised selection criteria and no further action was taken.

**February 2014**

Astellas Europe stated that its investigation in relation to this complaint highlighted that on 14 February 2014 an email was sent by a member of the Astellas UK medical team to the UK senior employee. This email asked whether or not 'we believe this group to have been appropriately selected'. A discussion took place between them whereby the UK medical employee was reassured with the criteria provided above (see under 17 October 2013).

The advisory board meeting was finally certified by Astellas on 26 February 2014, the day before the meeting started.

In response to the request to provide copies of any material used to debrief staff on the meeting at issue in Case AUTH/2747/1/15, Astellas Europe provided copies of a meeting report and a report on the results of a survey conducted with the meeting attendees.

**Allegations regarding its response in Case AUTH/2747/1/15**

Astellas Europe acknowledged that the suggested criteria in the presentation of February 2013 and the criteria provided in the email of 5 September 2013 and the email to the UK on 17 October 2013 were wholly inappropriate in that they described potential attendees as having the 'potential to be local product champions' and that they should be 'data naïve'; these were not suitable criteria for choosing advisory board attendees. These emails should not have been sent, given their content and the fact that the objectives for the advisory board and the criteria for selecting potential attendees had not yet been formally approved on Zinc. The communications were very disappointing as they clearly fell below the standard expected of Astellas employees and their compliance with the Code.

Concerns were raised internally about the inappropriate nature of the email and a revised, corrective email was sent in December 2013 to the affiliate contacts for the advisory board. Astellas Europe did not include the initial, unapproved, criteria in its response to the complaint in Case AUTH/2747/1/15 as these were not the ultimate final criteria communicated to the affiliates to identify health professionals that they considered should attend the advisory board; the criteria communicated

were those included in the letter to the Authority dated 6 February 2015 ie that they should be local experts in the field of mCRPC in their country, with personal experience of treating patients with mCRPC. These criteria were also included in the approval form for the meeting which was reviewed and approved by all relevant affiliates and ultimately certified by Astellas Europe signatories.

However, Astellas Europe acknowledged that the emails of 5 September and 17 October 2013, as well as the presentation from February 2013, were relevant to the complaint in Case AUTH/2747/1/15 and therefore the response to that complaint was incomplete. Astellas Europe submitted that that said, the selection criteria used by the UK was broadly similar to that provided to the Panel and the Appeal Board in its response to Case AUTH/2747/1/15.

Astellas Europe stated that it recognised that self-regulation relied on companies providing a full and frank disclosure in response to any complaint to the PMCPA and that by failing to do so in Case AUTH/2747/1/15 Astellas failed to maintain high standards, contrary to the requirements of Clause 9.1. In addition, the company acknowledged that its provision of an incomplete response to the previous case, although unintentional, had regrettably brought the industry into disrepute, in breach of Clause 2.

Astellas Europe recognised that all the UK nominations had been received before the corrective email of 12 December, however, as noted above, at the teleconference preceding the email of 12 December all affiliates were asked, in the light of the revised selection criteria, to reassess whether the health professionals already nominated were appropriate. Again, as noted above, none of the affiliates requested any changes to those originally nominated. Astellas Europe relied on the compliance reviewers in each of the affiliates to make this decision.

Given what Astellas Europe now understood in relation to the comments made by Astellas UK during the nomination process, it acknowledged that high standards had not been maintained, contrary to Clause 9.1. In addition, Astellas Europe noted that during the Appeal Board consideration of the report to the Appeal Board from the Panel in relation to Case AUTH/2747/1/15 Astellas was asked whether there was any sales force involvement in the nomination process; its response was that there was not. Although Astellas believed at the time that this was so, it acknowledged that this constituted the provision of inaccurate information to the Appeal Board and was likely to be considered to be an action that might bring the industry into disrepute.

In relation to the approval process for this advisory board, Astellas Europe pointed out that the Panel would have noted that the final certification of the meeting did not take place until the day before the meeting took place, after health professionals had been selected and invitations had been sent. Astellas Europe acknowledged that this might constitute a failure to maintain high standards. In addition, the medical signatory to one of the items in relation to the advisory board (the 'save the date' card) was not at the time registered with the GMC due to administrative reasons, or any equivalent non-UK organisation. The individual was however 'registerable' and had since re-registered with the GMC. The signatory was no longer a member of staff. The Panel might consider the fact that a medical signatory was not suitably registered at the time of certifying an item to amount to a failure to maintain high standards, in breach of Clause 9.1.

**Alleged dismissive manner in relation to Case AUTH/2747/1/15**

The complainant referred to attending training provided in relation to Case AUTH/2747/1/15 and that at a 'town hall' meeting, a very senior employee of Astellas discussed the case in a 'dismissive manner'. Astellas submitted that the company and the very senior employee personally, took the rulings in this case very seriously. Astellas stated that Healthcare Compliance (HCC) ran numerous compulsory training sessions for staff on the details of the case and the learnings taken from it. This training also included details on the requirements of advisory boards in general (a table was provided showing fifteen training dates and number of attendees at each session (total two hundred and five including seven agency staff)). All attendees were required to complete a mandatory validation quiz which was circulated via email. A copy of this training and validation quiz were provided. As Astellas Europe did not have a sales force, and given that the material was developed by HCC, members of which had detailed knowledge of the case and the wider Code requirements, Astellas Europe did not consider that the training required certification. It was, however, reviewed by legal, compliance and oncology colleagues before use.

For those who did not attend any of the sessions the training material was emailed to them with instruction to familiarise themselves with the content of the presentation and sample materials and complete a 'Read & Understood' form as well as the training validation quiz.

In addition, to ensure that employees fully understood the requirements in relation to advisory boards, a guidance document and tool kit had been developed and was sent to relevant Astellas Europe staff, and in June 2015 a moratorium on Astellas Europe advisory boards was put in place until September 2015 to allow staff to fully understand the Code and Astellas Europe's requirements in relation to such meetings. A copy of the email communication to staff in relation this was provided.

Astellas Europe stated that there was one town hall meeting since Astellas received the complaint in Case AUTH/2747/1/15 where the very senior employee was in attendance, held on 15 May 2015. The slides used at this meeting were provided. This meeting was specifically to discuss EMEA vision and strategy. Astellas submitted that it could be seen from the slides that Case AUTH/2747/1/15 was not discussed. In addition, there was an Astellas UK 'town hall' meeting, on 14 April 2015, at which the

very senior employee of Astellas Europe presented. Astellas Europe submitted that from the content, the case was not discussed.

However, in addition to the above training dates on advisory boards, Astellas stated that there were a number of occasions when the case and the rulings (both at the Panel and Appeal Board level) were discussed:

- Three Astellas Europe Quarterly Update Meetings took place in April 2015 with 28, 17 and 35 attendees, respectively. These were regular meetings at which recent Code cases were discussed. The invited audience was cross functional including legal, healthcare compliance, medical and marketing. At the meetings in April, the details of Case AUTH/2747/1/15 and the Panel ruling were communicated and discussed. The slides used at these three meetings and those disseminated to attendees and non-attendees were provided. The very senior employee attended one of the meetings and verbally summarised at the end of the session on the Panel's ruling.

- There were a number of briefing emails sent to Astellas Europe and affiliate staff in relation to the case and details of seven sent between April and July were provided. Astellas Europe submitted that it could be seen that all of the emails in relation to the case rulings and key learnings were from the Astellas Europe leadership team, and all emphasised Astellas' commitment to compliance and the importance of employees taking personal responsibility for this.

There were also a number of teleconferences in relation to the outcome of Case AUTH/2747/1/15 as below:

- Teleconference held on 5 May led by a senior employee, legal and compliance and attended by affiliate legal and compliance staff. The draft email to be sent to EMEA affiliates on 7 May was used as a script.
- Teleconference held on 6 May led by a senior employee, medical affairs and attended by affiliate medical directors and Astellas Operations medical directors. A script was used based on the draft 7 May email to EMEA affiliates.
- Teleconference held on 6 May 2015 led by a very senior employee of Astellas Europe and attended by the affiliate general managers. A script was used based on the draft 7 May email to EMEA affiliates.

In addition, four training sessions (for ninety-two attendees) were carried out in January-March 2015 in relation to a number of new and revised regional healthcare compliance standard operating procedures (SOPs).

In addition to the above training, all relevant staff also received the policies and processes through the Astellas electronic learning management system (LMS).

The very senior employee stated it was difficult to understand how he could be considered to have been dismissive of the outcomes of Case AUTH/2747/1/15. However, the complainant should have sought out the employee to clarify. This very senior employee had an 'open door' approach to receiving all feedback which was highlighted in all employee surveys. In view of the immediate steps taken to raise the awareness of all EMEA employees regarding the rulings in this case, including: mandatory advisory board training; advisory board moratorium and conference calls with all affiliate general managers, medical directors and legal/compliance staff, the very senior employee submitted that this demonstrated his commitment to compliance as opposed to any evidence of dismissiveness.

Since receiving this complaint, a number of Astellas Europe staff conducted interviews anonymously with individual members of staff that attended some of the training detailed above. In total, 12 members of staff were interviewed.

Astellas Europe submitted that nine of those interviewed considered that the individual took the matter seriously and did not discuss the case in a dismissive manner, as suggested by the complainant; two of those considered that he could have treated the matter more seriously. Three further members of staff considered that he was dismissive when discussing the case and the Panel's rulings.

Phrases used by those who considered that he was not dismissive were 'valuable [name] was there'; 'supportive'; 'not underplayed in any way'.

Other phrases recalled were 'we were trying something different'; 'the ruling shouldn't paralyse creativity'; 'there are large grey areas in application of the Code' and 'we don't want to stifle innovation'. Some of those who recalled these phrases were amongst those who did not consider that he was dismissive and some were amongst those who considered that the very senior employee should have taken the matter more seriously, which was an indication of the importance of perception vs intention in this matter.

Astellas Europe submitted that the above provided comprehensive detail in relation to the internal communications and training that was carried out to educate staff on the outcome and learnings from Case AUTH/2747/1/15 and the very senior employee's personal involvement with, and commitment to, this. Although there might be some comments to suggest that some staff interpreted a discussion in relation to this case as dismissive, this was certainly not his intention, and indeed other members of staff took the same comments in a positive way, and therefore the individual concerned did not consider that there had been a breach in that regard.

In response to a request for further information Astellas Europe acknowledged that the suggested criteria in the presentation of February 2013 and the criteria provided in the email of 5 September 2013 and the email to Astellas UK on 17 October

2013 were wholly inappropriate. Astellas Europe did not include the initial, unapproved, criteria in its response to the complaint in Case AUTH/2747/1/15 as these were not the ultimate final criteria communicated to the affiliates to identify health professionals that they considered should attend the advisory board. Astellas Europe stated that whilst its response of 23 July 2015 might suggest that there was a conscious decision not to include reference to the emails and presentation, this was not the intention and the wording could have been clearer. At no point during the preparation of its response to Case AUTH/2747/1/15 was there a discussion as to whether the emails of 5 September and 17 October 2013 or the presentation of February 2013 should or should not be submitted; these were not considered at all. The focus of the reply concerned the arrangements for the meeting, the number of attendees and the nature of the meeting, ie, whether it was promotional or non-promotional rather than primarily the criteria by which attendees were selected. Astellas Europe acknowledged that its investigation into this complaint was wholly inadequate in that regard.

When responding to Case AUTH/2747/1/15, Astellas considered the arrangements for the meeting and addressed the questions raised by the Case Preparation Manager. It considered that the rationale for choosing the attendees was addressed in the meeting approval form which was retrieved from the approval system. Astellas Europe stated it was regrettable that the emails of 5 September and 17 October 2013, as well as the presentation from February 2013, were not included in the response to this complaint which was incomplete. Astellas Europe submitted this was unintentional as it never set out to deliberately mislead. Astellas Europe focused on the materials within the ZINC system, but now recognised that it should have asked the agency and other Astellas staff involved if they had records of any relevant emails or materials and it was regrettable that this was not raised.

In November 2013, concerns were raised internally about the advisory board. Further discussions took place and a decision was taken to issue a corrective email to address the inappropriate criteria previously communicated to the affiliates and to change the working groups from international sessions to national working group sessions at the meeting. The corrective email was not, however, sent in November 2013 but was sent after the WebEx in December which was held with all affiliates participating in the advisory board and two emails sent on 12 December 2013. The emails were as follows:

1 One corrective email giving further details on the participants at the meeting in that they should be '... nominated for their expertise in the management of prostate cancer'. This attempted, in good faith, to correct and finalise the selection criteria for the invited health professionals; and
2 A further email dated 12 December which referred to the compliance implications in changing from international working group sessions to national working group sessions. The reference to compliance was also in relation to the revised criteria provided in the first email of 12 December, as during the WebEx affiliates were asked to reconsider those health professionals that had already been nominated, based on the revised criteria. No further information was documented with regard to this request and, as noted previously, no affiliates changed the health professionals they had nominated. Astellas submitted that it had a legitimate expectation that such corrective criteria would be implemented locally as per local affiliate approval processes.

Astellas Europe stated that discussions were held initially with Astellas UK when the original complaint letter, dated 15 January 2015, was received by Astellas UK. As the complaint related to the arrangements for an Astellas Europe-led meeting the UK affiliate and Astellas Europe had a joint meeting to discuss the complaint and which organisation should respond. The decision was that Astellas Europe should respond to the complaint and an email was sent to the Case Preparation Manager to that effect.

After this time, an interim member of staff at the UK affiliate at the time of receipt of the complaint was involved in preparing Astellas Europe's response to Case AUTH/2747/1/15, but this was only because at the time of the meeting he/she had a role at Astellas Europe.

From the recollection of Astellas UK and Astellas Europe staff in relation to any further UK involvement, there was a meeting when the draft response to the complaint was being finalised in which a UK medical employee recalled being asked to review the written criteria that Astellas Europe planned to submit in its response (ie that the health professionals selected worked in the field of mCRPC and had personal experience of treating patients with mCRPC) and confirm whether these were the criteria used by the UK. This was confirmed from memory.

Again at this point during the preparation of Astellas Europe's response to Case AUTH/2747/1/15 there was no discussion in relation to the email of 17 October 2013 sent by the agency to the Astellas UK senior employee and whether this should or should not be sent in the response; this was not raised or discussed at all and this might have been due to the significant time that had elapsed since the email was sent meaning that those preparing the letter of response had no awareness of or had simply forgotten about the existence of the email.

The UK health professionals who attended the advisory board were nominated in response to the email of 21 October 2013 from the UK senior employee, of which five UK health professionals in total attended, details were provided.

A business update was provided by the very senior employee of Astellas Europe to the UK town hall meeting in April. No discussion was held in relation to Case AUTH/2747/1/15 at this meeting.

The town hall meeting in May was to enable a senior employee from the Japanese Headquarters to present the new corporate global vision of

Astellas. No discussion was held in relation to Case AUTH/2747/1/15 at this town hall meeting.

Four individuals held interviews either face to face or over the telephone with 12 employees from Astellas Europe who had been present at the meetings where the very senior employee of Astellas Europe had spoken about the complaint and the Panel's ruling. These individuals briefed the interviewees on the second complaint and asked them to recall whether this individual made any comments in relation to Case AUTH/2747/1/15 and, if they did, specifically whether their recollection was that these comments were dismissive in relation to the rulings. They were also asked if they had any positive remarks to make in relation to any comments made when discussing the case. The guide used by interviewers was provided.

Due to the nature of the interview and the questions being asked, each interviewee was reassured that his/her comments would remain anonymous to the very senior employee and for this reason there was no formal report of each interview as such. Records were created following the interviews, and a collation was provided.

Astellas Europe stressed that while it now realised that the previous response was incomplete, there was never at any time any intention to be dishonest. Assumptions were made and subsequently proved to be incorrect. Astellas Europe reminded the Panel of the difficulty of recalling complex details a considerable time after the preparations for the Milan meeting.

**PANEL RULING**

The Panel noted that the complainant was anonymous and non-contactable. As stated in the introduction to the Constitution and Procedure such complaints were accepted and like all complaints, judged on the evidence provided by the parties. Complainants had the burden of proving their complaint on the balance of probabilities.

The Panel considered this case under the 2015 Code.

The Panel noted the outcome of Case AUTH/2747/1/15 and that the Panel had ruled Astellas Europe in breach of Clauses 2, 9.1, 12.1, 18.1 and 20.1 in relation to arrangements for a meeting. The Panel had also reported the company to the Code of Practice Appeal Board. The Panel's rulings were not appealed. The company attended for the consideration of the report. The Appeal Board required Astellas Europe to issue a corrective statement to UK attendees. This was issued on 1 July 2015.

The Panel noted that a further anonymous complaint had been made about the meeting at issue. It was not known whether the complainant was the same as for Case AUTH/2747/1/15.

The Panel noted that the meeting at issue in Case AUTH/2747/1/15 had been run by Astellas Europe. The complaint concerned arrangements for UK attendees. In this regard the Panel noted that Astellas UK was responsible for the acts/omissions of its affiliates including its UK based European headquarters. In the Panel's view this remained the position even if the UK based European affiliate had responded directly to the complaint. In its response to Case AUTH/2780/7/15 Astellas Europe explained that on receipt of the complaint in Case AUTH/2747/1/15 a joint meeting of Astellas UK and Astellas Europe had decided that the European affiliate should respond to the complaint. Correspondence in relation to Cases AUTH/2747/1/15 and AUTH/2780/7/15 had consequently been sent directly to Astellas Europe. The Panel noted the company's submission about the involvement of the UK company with the response to Case AUTH/2747/1/15 prepared by Astellas Europe. The Panel noted the position of Astellas UK in relation to the present complaint remained as set out above.

The Panel noted that the criteria used to select advisory board members to attend the meeting in question must stand up to scrutiny and relate solely to their ability to provide expertise to the company. The Panel considered that the email from the agency for Astellas Europe to send to certain affiliates dated 4 September 2013, the email from the agency to the Astellas Turkey affiliate dated 5 September 2013 and the email sent from the agency to the UK senior employee dated 17 October 2013 were wholly unacceptable in relation to the criteria to be used to identify potential advisory board members. All the emails and/or their attachments listed above referred to invitees being-mid to top level product opinion leaders with the potential to be local product champions within the relevant market and data-naïve customers ie those who had not been involved in any Astellas Europe or national/local advisory board meetings prior to the Pan EU Expert Meeting.

The presentation to the Oncology Steering Committee (5 February 2013) which accompanied the email of 4 September 2013 [Following notification of the Panel's rulings, Astellas Europe stated on 28 August that this was not so] referred to the success of the Pan – European Uro-oncology Advisory Board held in Barcelona in November 2012. It stated that the proposed structure of future meetings was discussed/agreed by a UK medical employee. This presentation referred to the aims and suggested target audience for 13/14 pan European advisory board meetings as:

**'Objectives for meeting**

- Increase Astellas' profile in the field of oncology
- Communicate Astellas' strategy and oncology pipeline to key target customers
- Communicate Xtandi and tivozanib data and common set of messages to EU affiliates' key target customers
- Gain an increased understanding of the current landscape in RCC and prostate cancer & the challenges Astellas will face when launching Xtandi and tivozanib in the EU

**Target audience for meeting**

- Mid – top level product OLs – those with the potential to be local product champions within the relevant EU markets
- Data – naïve customers, ie those who have not been involved in any APEL or national/local advisory board meetings prior to the pan EU ad board meeting
- 10 per affiliate: 5 prostate/Xtandi and 5 RCC/ tivozanib*

*Turkey – 10CRPC OLs.'

The emails sent to the UK affiliate which reflected the selection criteria set out above, the email which the UK senior employee forwarded to UK managers, and the responses from this team dated 17, 21, 22 and 24 October compounded the unacceptability of the arrangements. In that regard the Panel noted the email from one of Astellas UK staff identifying health professionals who met these unacceptable criteria included '[city] is one of … main key accounts', '… one of our high users and would respond well to such a meeting…', '… is influential at a [city] level and more and more nationally with time' and 'This is a business move … barely sees industry, not using prechemo abi and once using he rarely changes'. The reserve nominations included '… I believe he has the reputation with us for being an abi man, however, this would give us the opportunity to convert him to the new way and '…is on our list and is influential, and would be good to engage at this level'.

The Panel did not accept Astellas Europe's submission in its initial response in the case now under consideration that its provision of an incomplete and in the Panel's view misleading response was unintentional given Astellas' decision not to include the unapproved criteria following the dispatch of what Astellas Europe described as a revised corrective email (December 2013). The Panel noted Astellas Europe's submission that it did not include the initial unapproved criteria in its response to Case AUTH/2747/1/15 as these were not the ultimate final criteria communicated to affiliates. It further noted the company's submission that there was no consideration at all as to whether the emails of 5 September and 17 October should be submitted as part of its response to the previous case, Case AUTH/2747/1/15. Astellas Europe acknowledged that its investigation into that complaint was inadequate.

The Panel was extremely concerned that Astellas Europe appeared to consider that ultimate revised final selection criteria had been communicated. In the Panel's view that was not so. Neither of the two emails dated 12 December sent from Astellas Europe contained revised selection criteria. That sent at 16.35, 'subject: Pan Eu expert meeting' discussed the meeting in relation to its objectives, content, format, timing and location. The Panel considered that the email described, *inter alia*, what the selected participants were expected to do. It did not make it at all clear that the original selection criteria had changed. Similar criticisms applied to the email sent at 16.41. Contrary to the impression given by Astellas Europe this email referred only to compliance in relation to the change from international working group to national working group. The final paragraph asked affiliates to discuss the meeting with the compliance/Zinc manager. However again this paragraph did not refer to selection criteria revised or otherwise and within the context of the letter appeared to refer to the change to the international working group highlighted in the email. The Panel noted Astellas Europe's submission that the teleconference held on 12 December discussed the revised selection criteria for attendees. In the Panel's view this should have been made abundantly clear in the emails of 12 December. Astellas had not provided detailed information regarding the discussion on the teleconference. Given its comments above the Panel was not at all surprised by Astellas Europe's submission that none of its affiliates had subsequently requested any changes to those nominated as attendees. It was hard to understand why such a fundamental change to the selection criteria had not been made clear at the outset in either of the emails.

The Panel noted that the original selection criteria as set out in the emails of 4, 5 September and 17 October and the presentation to the Oncology Steering Committee dated 5 February 2013 were directly relevant to the subject matter of the complaint in Case AUTH/2747/1/15. In the Panel's view Astellas Europe had therefore provided not only an incomplete response to that complaint but also a misleading one.

The Panel noted Astellas Europe's submission that the final certification did not take place until the day before the meeting took place (26 February 2014) after health professionals had been selected and invitations sent.

In addition to the provision of an incomplete response, the Panel noted Astellas' submission that it was now apparent that its representatives had misled the Appeal Board when the report was considered as the UK sales force had been involved in the nomination process.

The Panel noted Astellas Europe's submission that concerns had been raised in November 2013 and that in January 2014 it had received an anonymous complaint about the meeting which had been dealt with by the issuing of the revised selection criteria and thus no further action was taken. The Panel noted its comments above about the revised selection criteria and their communication. The Panel also noted that Astellas Europe's response to the Panel's request for further information was different to its initial submission in relation to whether the company knew about the emails and the changes to the selection criteria for attendees and had decided not to provide them or whether the company had not asked staff for materials etc other than those in the Zinc system. In the Panel's view Astellas had either not paid sufficient attention to ensuring that all relevant information had been supplied in its response to Case AUTH/2747/1/15 or had made a conscious decision to omit relevant details from that response. The Panel noted Astellas Europe's most recent submission in this regard that it had not considered the material at all.

The Panel was extremely concerned and disappointed by the conduct of Astellas Europe

and Astellas UK. The integrity of self-regulation relied upon the provision of complete and accurate information by pharmaceutical companies. The Panel considered that the failure to provide all the information and the misleading nature of what was submitted by Astellas Europe in Case AUTH/2747/1/15 meant that high standards had not been maintained. A breach of Clause 9.1 was ruled as acknowledged by Astellas Europe. The circumstances brought discredit upon and reduced confidence in the pharmaceutical industry. The Panel ruled a breach of Clause 2 as acknowledged by Astellas Europe. Clause 2 was a sign of particular censure.

In relation to the allegations about the discussion of the case by a very senior employee of Astellas Europe, the Panel noted the comments made by staff interviewed about meetings which the individual had attended. It appeared that these were not 'Astellas town hall' meetings as stated by the complainant. It was not clear what the meeting referred to by the complainant was but the complaint was clear it was a meeting where the very senior employee discussed the matter. The Panel was concerned that the interview guide for discussion with employees appeared to be biased and designed to encourage staff to confirm that they were impressed by the training and the 'Tone from the top'. Bearing in mind the difficulties for staff in being critical of senior management, the Panel was very concerned that the comments on the outcome of Case AUTH/2747/1/15 were viewed as dismissive and/or that the matter was not taken seriously enough. This was compounded by the serious nature of that case. The details set out in the collated interview feedback master document appeared to be different to those provided elsewhere in the company's response. Nonetheless it was clear that despite the content and tone of the interview guide, certain staff were concerned about the impression given. The Panel was also concerned that staff recalled the phrases 'we were trying something different' and 'there are large grey areas in application of the code'. The Panel disagreed with the latter comment in relation to Case AUTH/2747/1/15 as the requirements for advisory boards and other such meetings were clear in the Code, supplementary information and guidance issued by the PMCPA.

The Panel considered, given the seriousness of Case AUTH/2747/1/15, it was completely unacceptable in the companies' discussion of that case for a very senior employee of Astellas Europe to give any impression that he and/or the company was dismissive of the Panel's rulings and the Appeal Board's consideration of the report from the Panel. The Panel considered that in this regard high standards had not been maintained and ruled a breach of Clause 9.1. In addition the Panel considered that the circumstances brought discredit upon and reduced confidence in the pharmaceutical industry. The Panel ruled a breach of Clause 2. These rulings were appealed by Astellas Europe.

The Panel considered that the circumstances regarding the failure to provide comprehensive, accurate information, the misleading nature of the submissions in Case AUTH/2747/1/15, the relevance of the omitted material and the discussion of the outcome of the case by Astellas Europe raised serious concerns about the companies' procedures. In this regard the Panel noted Astellas Europe's submission about its certification of the arrangements the day before the meeting in question. It also noted the Appeal Board's comments when considering the report from the Panel in Case AUTH/2747/1/15 that the company's standard operating procedures were either unclear or not followed and its questions over the rigour of Astellas Europe's certification process.

This case also raised fundamental concerns regarding Astellas Europe and Astellas UK's approach to compliance and self-regulation.

The Panel noted its comments above regarding the position of Astellas UK and Astellas Europe in relation to this case. The Panel considered that its serious concerns warranted reporting Astellas Europe and Astellas UK to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure for the Appeal Board to consider in relation to Paragraph 11.3 of the Constitution and Procedure.

During its consideration of this case the Panel noted the meeting at issue was the third such meeting held by Astellas Europe. There had been no complaint about the previous two meetings which had taken place before and immediately after the initial marketing authorization of Xtandi in the treatment of adult men with metastatic castration-resistant prostate cancer whose disease had progressed on or after docetaxel therapy. The third meeting, the one at issue in Case AUTH/2747/1/15, was held prior to the grant of the marketing authorization for a new indication for the treatment of adult men with metastatic castration-resistant prostate cancer who were asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy was not yet clinically indicated. On the basis of the new information which came to light in Case AUTH/2780/7/15 the Panel was concerned about the arrangements for the two previous meetings held in 2012 and 2013 and the company's response to Case AUTH/2747/1/15. However there was no complaint about these two meetings, either in this case or the previous case. The Panel requested that Astellas be advised of its views.

**APPEAL BY ASTELLAS EUROPE**

Astellas Europe appealed the Panel's rulings of breaches of Clauses 9.1 and 2 in relation to the allegation that a very senior employee had discussed the Panel ruling in Case AUTH/2747/1/15 in a dismissive manner.

Astellas Europe noted in its response to the complaint there were a number of occasions where this individual was present when Case AUTH/2747/1/15 was discussed; each meeting was different in relation to the number of attendees, audience, format and his personal role and involvement. There were a number of key points that should be taken into consideration as detailed below.

Astellas Europe noted that the complainant alleged that a very senior employee had discussed Case AUTH/2747/1/15 in 'a very dismissive manner'. One definition of 'dismissive' was: 'contemptuous, scornful, disdainful, insulting, sneering, derisive; He was highly dismissive of the report'. The Oxford English Dictionary noted that dismissive as an adjective was defined as 'showing that you feel something is not worth consideration'. These were strong terms which could also be subjective. None of these words were used by any of the Astellas Europe staff who were interviewed during its preparation of its response to Case AUTH/2780/7/15.

Astellas submitted that 'Tone from the Top' was critical in any compliant organisation and it was an aggregate of continuous, transparent and consistent activities, policies and procedures, communications in various forms and formats, oversight by a governance structure (consisting of the head of the organisation and a senior cross-functional management team), auditing and monitoring and responding to deviations and enforcement of standards. Critical to this was the importance of engagement of senior leadership in demonstrating an organisation's approach to compliance. 'Tone from the Top' was not defined as a single activity, communication or conversation. The individual concerned took a very structured approach to this in leading an organisation of approximately 4,000 employees across the regions of Europe, Middle East and Africa as well as a very senior role at Astellas Pharma Europe Operations. Astellas Pharma Europe Operations consisted of approximately 350 employees (encompassing 32 nationalities) and approximately one quarter did not have English as their first language. Therefore, in communicating important messages, various channels were used eg, email, face-to-face and teleconferences. These communications were carefully prepared to ensure a consistent message. It was in this context that the alleged comments must be considered.

Astellas Europe noted that the individual had adapted his communication style to take into consideration the audience, including both non-native and native English speakers and he therefore tended to be very factual and even-tempered. This might create varying nuances and interpretations with both native and non-native English speakers. Perhaps the complainant was expecting him to exude more 'fire and brimstone' in relation to the circumstances and rulings in Case AUTH/2747/1/15. The individual did not consider this appropriate as he had simply wanted to convey to the audience in each of his communications the fact that Astellas had got it wrong, the seriousness of the case and the necessary 'lessons learned'. Finally, he conveyed the need to fix the problem and move forward in a compliant manner; he wanted staff to understand that if they learnt from mistakes they could confidently make the compliance decisions they needed to make on a day-to-day basis.

Astellas Europe submitted that the individual concerned had been highly engaged in all of the communication activities around Case AUTH/2747/1/15, which took place with his strong and open support (as previously stated and shown below). If any individual took as dismissive any of his comments, this should be seen as a misunderstanding. As an aggregate, the various communications and activities that took place in relation to the rulings in the case demonstrated strong leadership and personal support for Astellas Europe's positive approach and attitude to healthcare compliance. The very senior employee also held a town hall meeting that took place for Astellas Pharma Europe and UK staff on 30 July where both cases were referred to (slides with notes were provided):

| Activity | Date |
|---|---|
| Advisory Board training (15 sessions) | 5 May-12 June 2015 |
| Astellas Pharma Europe Quarterly Compliance Update (3 sessions) | 8, 15 and 22 April |
| Panel ruling communication | 8 April 2015 |
| Key Learnings teleconferences (3 sessions) | 5 and 6 May 2015 |
| Key Learnings communications (emails to Astellas Pharma Europe and the UK Affiliate and to EMEA affiliates) | 7 May 2015 |
| Appeal Board ruling communications (emails to Astellas Pharma Europe and the UK Affiliate and to EMEA affiliates) | 28 May 2015 |
| Communication on the Advisory Board Moratorium | 2 June 2015 |
| Communication on the publication of the case report (emails to Astellas Pharma Europe and the UK Affiliate and to EMEA affiliates) | 1 July 2015 |
| Communication on the issue of the Advisory Board Tool Kit | 1 July 2015 |
| Astellas Pharma Europe and UK Affiliate town hall | 30 July 2015 |

Astellas Europe discussed the meetings at which some of those interviewed considered that the very senior employee had been dismissive (the Quarterly Compliance Update and the Advisory Board training). At these meetings, rather than leading them, the individual attended in person as a trainee.

At the Quarterly Compliance Update meeting in April 2015, Astellas Europe submitted that the individual concerned recalled, at the end of the meeting, discussing with all the attendees that one key aspect of the case was that Astellas had failed to establish the Milan meeting as non-promotional, and that the other issues such as unacceptable payments flowed from that finding. This discussion was not intended to be dismissive of the Panel's ruling. The individual was merely trying to convey the concept that if you got this aspect wrong then all of the other arrangements and details were likely to be inappropriate. He reminded attendees that although they worked in an

environment that required creativity and innovation, this must be done in a compliant manner, and referred specifically to the Panel ruling in that holding multiple simultaneous local advisory boards overseas in one central location was not necessarily unacceptable, but the 'devil was in the detail' and the execution and content must be compliant. The individual then opened the floor to any questions and reiterated what was said on the slides presented at the meeting, that further information would be provided during the compulsory training on advisory boards. The relevant slides were provided.

Astellas Europe submitted that in the advisory board training meeting held in June 2015, there were four attendees and the trainer; two of the attendees had only recently joined the organisation and this was the first time that the very senior employee had interacted with these two individuals. The training session was specifically designed to be interactive to enable the trainees to ask questions for clarity in order to improve future planning and execution of advisory boards. During this training, which referred to the aspects of the case, the very senior employee raised questions with the trainer on the detailed learnings of the rulings, especially that the Q&A section of the advisory board was not considered part of the advice gathering aspect of the meeting. The very senior employee was not dismissive, to the contrary, he was trying to understand the ruling in order that he could apply the learnings. Once again, the same key aspect was discussed ie, the failure to establish the meeting as non-promotional and the issues flowing out of this. The tone and manner when the very senior employee was speaking at this meeting was that of a trainee rather than as one leading the meeting.

The Panel had noted the very senior employee's comment that 'there are large grey areas in the application of the Code' and disagreed with this comment in relation to advisory boards. Astellas Europe submitted that this comment was not made in relation to advisory boards nor the specific case being discussed. Astellas fully agreed that the requirements for advisory boards were very clear in the Code, as well as supplementary information and guidance issued by the Authority. However, this comment was made in relation to the Code in general as the new Code had been published for 2015 and was due to come into full effect around the time of communicating the learnings from Case AUTH/2747/1/15. As this was discussed in a learning environment, the very senior employee encouraged his colleagues to question any areas of the Code that they did not understand and seek advice, if necessary.

Astellas Europe trusted that it had put into context any misunderstanding that might have arisen in relation to the discussion of the rulings in Case AUTH/2747/1/15 and its wider approach to healthcare compliance. The concerns of individuals about whether the very senior employee was dismissive or could have taken the rulings more seriously perhaps were more of a disconnect between communication style/delivery and that which the individual might have expected given the subject matter. Taken as a whole, the volume of communication and training that took place following the Panel's and Appeal Board's ruling in relation to this case, as opposed to an alleged isolated comment that appeared to have been misconstrued, demonstrated the very senior employee's commitment to, and leadership in, compliance with the Code, and thus Astellas Europe submitted that that there had been no breach of Clauses 9.1 or 2 in that regard.

Finally Astellas Europe submitted that the 'Tone from the Top' the very senior employee had set for the company had been one of personal engagement, support, transparency and strong leadership to ensure employees understood the importance of healthcare compliance. At the Appeal Board meeting, in addition to providing a short presentation in relation to its appeal, Astellas Europe would also provide the Appeal Board with information on the key compliance activities that had been and were taking place since the conclusion of Case AUTH/2747/1/15.

**APPEAL BOARD RULING**

The Appeal Board noted that the appeal related to the complainant's view that a very senior employee of Astellas Europe discussed the outcome of Case AUTH/2747/1/15, in a very dismissive manner.

The Appeal Board noted that the interview guide used for staff who had attended a meeting with the very senior employee stated 'From my recollection of that [telecom] [meeting] I was not aware of any dismissive comment(s) …'. It then stated 'In fact [I was impressed] by the mandatory training and "Tone from the Top" reflecting the importance of compliance at Astellas'. The Appeal Board considered that the interview guide was biased. The Appeal Board noted the response from the Astellas representatives at the appeal that the interview guide was used by interviewer to 'get the conversation started'. However, the Appeal Board queried whether this was so given that it requested a 'Name', 'Title' and included a signature clause at the bottom. In the Appeal Board's view, given the content of the interview guide and that the interviews were overseen by a senior director the interviewees would be left in no doubt what was expected of them. The Appeal Board noted that despite the strong steer of the guide some interviewees still considered a more cautionary tone might have been conveyed, one expressed surprise that the ruling was not being treated seriously. One interviewee used the word 'belittled'. One considered that the very senior employee was dismissive, referred to the breaches as technicalities and when referring to the breaches stated that the organisation of the advisory board was not non-compliant but rather its execution. At the Appeal Board hearing the individual was very clear that he had not used the word 'technicality'. The Appeal Board noted that in the collated interview feedback master document some interviewees had adopted phrases closely similar to those in the interview guide. The Appeal Board noted that it had only received collated interview responses from twelve employees and yet there was still evidence that the very senior employee had been

dismissive or that the matter was not taken seriously enough. The Appeal Board also noted the company's submission that the individual attended the advisory board training as a trainee which was reflected in his tone and manner.

The Appeal Board considered that the communications concerning the outcome of Case AUTH/2747/1/15 did not unequivocally convey, as submitted by Astellas Europe in that case, that it had agreed that the execution of the Pan-European Advisory Board should have been conducted to a higher standard and it did not meet the criteria for advisory boards, as required by the Code and its standard operating procedures (SOPs). The Appeal Board noted that to convey the seriousness of the matter to a broad audience it was important that such communications were abundantly clear. The Appeal Board was particularly concerned about the wording for the teleconference script used by the very senior employee which stated that 'Unfortunately, due to poor execution of the arrangements and materials, the perception of the meeting by the complainant and by the PMCPA (the UK code authority), was such that Astellas was ruled in breach of a number of clauses of the Code.' (emphasis added). The Appeal Board considered that 'perception' could be seen by some as ambiguous and implied that this was other than a clear breach of the Code.

The Appeal Board was concerned that staff recalled the phrases 'we were trying something different', 'the ruling shouldn't paralyse creativity' and 'there are large grey areas in application of the Code'. The representatives from Astellas at the appeal stated that these phrases had been used to relate to the Code in general and to raise discussion. The Appeal Board considered that for the very senior employee to make such comments when cascading the outcome of Case AUTH/2747/1/15 sent a confusing message. In that regard the Appeal Board noted that the requirements for advisory boards and other such meetings were clear in the Code, supplementary information and guidance issued by the PMCPA. The arrangements for Astellas Pan-European Advisory Board were unacceptable and clearly in breach of the Code and the company had accepted this. The company did not appear to have clearly explained the gravity and seriousness of the breaches, the report from the Panel to the Appeal Board and corrective statement in its communications.

The Appeal Board considered that on the balance of probabilities there was evidence to show that the very senior employee of Astellas Europe had given the impression that he was dismissive of the Panel's rulings and the Appeal Board's consideration of the report from the Panel. In this regard high standards had not been maintained and the Appeal Board upheld the Panel's ruling of a breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board considered that the impression given brought discredit upon, and reduced confidence in, the pharmaceutical industry and it upheld the Panel's ruling of a breach of Clause 2. The appeal on this point was unsuccessful.

**COMMENTS FROM ASTELLAS EUROPE ON THE REPORT FROM THE PANEL**

Astellas Europe contacted the PMCPA in September to advise that it had recently discovered information which the company wished to provide to the Appeal Board in relation to its consideration of the report from the Panel. The Director of the PMCPA referred the matter to the Chairman of the Appeal Board who, agreed that Astellas Europe could submit further information in relation to the report. The information did not relate to Astellas UK.
Astellas Europe stated that it had conducted a number of staff interviews as part of its continued human resources investigation into the complaint and an email had been discovered which it considered to be the source of the concerns that were raised in November 2013 about the advisory board at issue in Case AUTH/2747/1/15. Astellas Europe referred specifically to the wording of its response to the complaint where it stated 'In November 2013, concerns were raised internally about the advisory board'.

Astellas Europe submitted that it was important for the Appeal Board to be made aware of the content of this email when it considered the report from the Panel in Case AUTH/2780/7/15. The email, from a senior employee at Astellas Europe was dated 26 October 2013 and indicated that the sender was instructing the team to remove an unacceptable objective for the advisory board from the meeting agenda in order to 'smooth the passage' of the meeting through the approval process, but unfortunately made it clear that this was still a key objective of the advisory board.

Astellas Europe noted that as background, an email entitled 'Draft agenda for the Feb Pan EU Advisory Board Meeting' was sent by its agency to various members of the oncology business unit on 24 October 2013 at 22:00. Attached to this email was a draft agenda for the meeting that was the subject of the complaint in Case AUTH/2474/1/15. On the same day, at 22:48, a member of the oncology business unit replied with a revised agenda attached. The revised agenda contained tracked changes; the objective 'Communicate the role of uro-oncology as a major component of the Astellas Oncology strategy' had been crossed out, with the comment 'Should this really be an objective of an ad board?'.

The email of 26 October 2013 from the senior employee to the agency stated, *inter alia*:

> 'Re Objective about communicating our Oncology strategy, agree let's take off to smooth the passage through Zinc although be clear amongst us that communicating our commitment/strategy is a clear objective of this type of meeting which we will need to cover off as in the agenda.'

Astellas Europe submitted that this indicated that there was a conscious decision on the part of one individual to circumvent the established approval process in order to incorporate an unacceptable objective in to an advisory board ie to use the

meeting to establish relationships with health professionals and communicate the company's strategy in a particular therapy area.

Astellas Europe submitted that the email appeared to be the trigger for the activities that took place in late 2013 to reassess the meeting and address the concerns raised. Two of the four members of staff in receipt of the email of 26 October 2013, whilst not sharing or discussing the email directly with anyone, raised their concerns about the meeting. The activities in November and December 2013 were as a consequence of this in an attempt to correct the issues raised eg the teleconference and emails of 12 December 2013.

Astellas Europe as an organisation stated that it was not aware of the emails until 22 September 2015 which was why they were not submitted in the company's response to Case AUTH/2780/7/15. This was particularly disappointing, given that the individual in question was asked for all information relevant to the meeting at issue in Case AUTH/2747/1/15. As a result of this discovery further investigations were on-going.

Astellas Europe stated that the Panel's ruling in Case AUTH/2780/7/15 might still have been the same, given that it recognised the inadequacies of the initial investigation to the complaint in Case AUTH/2747/1/15. However it was important that the Appeal Board was notified of the additional information, which the company submitted was crucial to the case.

At the consideration of the report the representatives from Astellas Europe and Astellas UK stated that the companies recognised that the investigation and response to Case AUTH/2747/1/15 was inadequate. The companies submitted that there was no dishonesty or deliberate attempt to mislead. The investigation had identified that an individual senior member of staff central to this situation withheld key information from Astellas Europe, the Panel and Appeal Board. Immediate action had been taken to address the conduct of this senior member of staff. Astellas incorrectly assumed that there was no sales involvement in nominating UK health professionals to attend the advisory board and therefore it unintentionally provided inaccurate information to the Appeal Board.

Astellas accepted the Panel's rulings of breaches of the Code and deeply regretted that it had brought disrepute on the pharmaceutical industry.

Astellas Europe stated that it had already undertaken a number of measures and gave details of its key compliance activities since the completion of Case AUTH/2747/1/15. These included: internal audit preparation; full gap analysis of healthcare compliance program by external consultant at Astellas Europe; review and revision of existing standard operating procedures (SOPs) and policies, development of new SOPs including: Astellas Europe - Complaint Handling SOP and Deviations SOP, UK Affiliate – Advisory Board SOP, advisory board moratorium within Astellas Europe until 31 December 2015; all UK led advisory boards required medical director approval in addition to routine approvers, communication on publication of case report, communication on advisory board toolkit/ templates within Astellas Europe; approval for further increase in healthcare compliance headcount; town hall meetings.

**APPEAL BOARD CONSIDERATION OF THE REPORT FROM THE PANEL**

The Appeal Board noted the Panel's comments and rulings including its ruling of a breach of Clause 2 and the outcome of the appeal where the Appeal Board upheld a second Panel ruling of a breach of Clause 2. The Appeal Board was extremely concerned about the approach to compliance and poor communication across Astellas Europe and Astellas UK.

The Appeal Board noted the Panel's comments that the original selection criteria for Astellas Europe's Pan-European Uro-oncology Advisory Board Meeting were directly relevant to the subject matter of the complaint in Case AUTH/2747/1/15 yet these had not been provided by the company in its response to that case.

The Appeal Board was also very concerned about why the email dated 26 October 2013, sent by the senior employee of Astellas Europe was not previously provided. The Appeal Board noted from Astellas that two recipients of the email had raised concerns about the meeting back in 2013 but they had not disclosed the email itself. The representatives from Astellas at the consideration of the report stated that the email was handed to senior management by one or more employees on 22 September 2015. The Appeal Board was concerned that such relevant information had not surfaced until this late stage.

It appeared to the Appeal Board that employees did not feel confident to raise issues with management. It noted that the company had received an anonymous complaint but the company considered this had been dealt with. At least three senior members of staff could have raised their concerns and did not.

The Appeal Board was very concerned about the culture of the organisations and that despite a prior internal complaint raising the issue it had taken two complaints under the Code and a late submission of evidence in the present case to produce comprehensive information concerning selection of the delegates for the meeting at issue.

The Appeal Board was concerned that the arrangements had been reviewed and approved by the UK affiliate. Astellas Europe certified the arrangements the day before the advisory board at issue took place. The Appeal Board noted that there was no UK medical director at the relevant time and further that due to a number of relevant vacancies at Astellas Europe, the European company relied on the UK affiliate for guidance. '[Post meeting note: Subsequently, on notification of the Appeal Board ruling, Astellas advised that it did have a UK medical director in post at the relevant time]'.

The Appeal Board considered that Astellas had provided not only an incomplete response to the original complaint but also a misleading one. The Appeal Board considered that self-regulation relied upon the provision of complete and accurate information by pharmaceutical companies. Astellas's omission was totally unacceptable. The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure that both Astellas Pharma Europe and Astellas UK should be publicly reprimanded for this failure.

The Appeal Board noted that the UK health professionals who attended the meeting had been provided with a corrective statement and a case report which was misleading. This was totally unacceptable. Consequently the Appeal Board decided, in accordance with Paragraph 11.3 of the Constitution and Procedure, to require Astellas Europe and Astellas UK to issue a corrective statement to all the UK attendees at the meeting to clarify the position. The corrective statement should refer to both case reports. Under Paragraph 11.3 details of the proposed content and mode and timing of dissemination of the corrective statement must be provided to the Appeal Board for approval prior to use. [The corrective statement appears at the end of the report.]

The Appeal Board also decided that, given all of its concerns about the conduct of Astellas as set out above, to require, in accordance with Paragraph 11.3 of the Constitution and Procedure, an audit of both Astellas Pharma Europe and Astellas UK's procedures in relation to the Code. The audit would take place in December 2015. On receipt of the audit report, the Appeal Board would consider whether further sanctions were necessary including the possibility of reporting the companies to the ABPI Board of Management (Paragraph 12 of the Constitution and Procedure).

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas Pharma Europe and Astellas UK were each audited in December 2015 and on receipt of the report of the audits, the Appeal Board noted that it included separate findings and recommendations for each company as well as joint findings and recommendations. The Appeal Board was extremely concerned that despite a very critical report that highlighted numerous serious concerns including the companies' cultures and a reference to Astellas Europe's institutional failure with respect to compliance, neither Astellas Europe nor Astellas UK provided any detail on when and how each would address those concerns.

The Appeal Board decided that both companies should be re-audited but before setting a date for such, each should provide a detailed compliance action plan and a comprehensive response to the recommendations in the report of the audits. The Appeal Board discussed further sanctions including, again, whether there should be a report to the ABPI Board. The Appeal Board concluded that on receipt of the report for the re-audits it would decide whether further sanctions were necessary.

In February 2016 the companies subsequently provided a further detailed response as requested. The Appeal Board considered that both companies had set themselves a number of compliance objectives and sufficient time would be needed for these to be completed or get underway. In that regard the Appeal Board decided that Astellas Pharma Europe and Astellas UK should each be re-audited in September 2016 by which time the Appeal Board expected both companies to be able to demonstrate significant improvement.

**CODE OF PRACTICE PANEL FURTHER CONSIDERATION**

During the Code of Practice Appeal Board's consideration of the audit reports for Astellas Europe and Astellas UK (25 February 2016) it noted a letter from Astellas Europe (17 February) which stated that new information had been discovered as a result of further investigation which would assist the understanding of the full circumstances of these cases. The company would send the information to the PMCPA. The Appeal Board requested that the Director followed this up.

On receipt of further information from Astellas Europe the original Panel was reconvened to consider the matter.

**FURTHER INFORMATION FROM ASTELLAS EUROPE**

Astellas Europe set out the organisational restructure in relation to compliance. A new function, Ethics & Compliance, with a global reporting structure, would be established effective from 1 April 2016. This was reflected at Astellas Europe by dividing 'Legal & Compliance' into 'Ethics & Compliance, EMEA' and 'Legal, EMEA'. The Ethics & Compliance function would report outside of Astellas Europe to Japan, thus providing a much more robust compliance structure with no reporting line in to senior management at Astellas Europe. Astellas was now recruiting a dedicated senior healthcare compliance director to report in to the Ethics & Compliance function.

Astellas Europe stated that Astellas Pharma Inc, with the assistance of external counsel, conducted a thorough internal investigation into the circumstances leading up to the meeting in Milan (Case AUTH/2747/1/15) as well as matters that led to Astellas Europe providing an incomplete and misleading response (Case AUTH/2780/7/15). The results of the completed investigation had been shared with Astellas. The majority of the report confirmed facts already known to the PMCPA and it revealed further information that appeared to have been known to a number of members of Astellas Europe senior management but had not, to date, been shared with the Authority. The details were provided below.

Astellas Europe was notified of the complaint in Case AUTH/2747/1/15 on 15 January 2015 and its initial response to this complaint was submitted to the PMCPA on 6 February 2015. The interviews conducted during the investigation, as well as a review of email accounts of certain individuals,

had revealed that, on 30 January 2015, whilst the response to the PMCPA was being prepared, an email was sent by a member of the oncology business unit to his line manager. This email, *inter alia*, referred to the email of 5 September 2013 ('selection criteria email') sent by a senior employee to Astellas affiliate employees (the email that became the subject of the complaint in Case AUTH/2780/7/15) and expressed concern that the response to the PMCPA under preparation would not disclose the selection criteria email. The 30 January 2015 email referred to the need 'to provide the PMCPA with a full and truthful response to the complaint made and not to mislead or deceive them'.

The employee who received the 30 January email raised it with very senior employees all of whom were involved in drafting the response which stated, *inter alia*, that 'we have no intention to mislead or deceive and will provide an appropriate response to the PMCPA'. Astellas Europe considered that this demonstrated that the very senior employees quite clearly addressed the question of whether or not to include the original selection criteria for health professionals invited to attend the Milan meeting in the response to Case AUTH/2747/1/15 and deliberately decided to omit such information. This was, of course, wholly unacceptable.

A new President of Astellas, EMEA Operations, was appointed on 1 April 2016. Very senior managers had left the organisation.

Astellas Europe stated that it remained committed to continuing the significant changes that were required to address the issues leading to the audit in December 2015 and those noted during that audit. It remained committed to operating with the highest sense of ethics and integrity.

Following a request from the PMCPA for further information which referred to the need to inform the Appeal Board of the position and that this might be by way of a report under Paragraph 8.2 of the Constitution and Procedure, Astellas Europe provided more information including the report by external counsel.

**FURTHER INFORMATION FROM ASTELLAS EUROPE**

The investigation report, prepared by external counsel which was provided to the investigation committee of the Astellas Europe Board, contained privileged material, notably summaries of the content of interviews conducted with employees. All material information gathered in the course of these interviews was communicated within the findings.

In response to the PMCPA question as to how and when the email of 30 January 2015 was raised by an employee with senior management and how Astellas Europe knew this, the company stated that the investigation team learned from an interview with its employee that the email was brought by him/her into an impromptu meeting between him/her and senior employees.

During an interview with the investigation team, a very senior employee corroborated that the email had been discussed at this meeting and that, also at this meeting, he/she had typed the response to it. Astellas Europe understood that this very senior employee read the response out to the group as he/she typed it.

Some further documentation about the 30 January 2015 email was reviewed by the investigation team. It appeared that Astellas Europe's human resources department, did not understand the significance of the email.
In response to another request from the PMCPA, Astellas Europe stated that a number of staff including very senior staff had left the company.

Astellas Europe stated it was confident that, with the organisational restructure resulting in the creation of the Ethics & Compliance function, the new personnel in place and the action plans developed in response to the issues identified during the PMCPA audit, it would be able to address the PMCPA's concerns. Most critically, the new structure and the declared plan of actions would considerably strengthen Astellas Europe's compliance governance and oversight.

**PANEL RULING**

The Panel noted the circumstances surrounding Cases AUTH/2747/1/15 and AUTH/2780/7/15, the reports to the Appeal Board, the findings of the audits, particularly those relevant to Astellas Europe, and the additional information now provided by Astellas Europe. The companies were to be re-audited in September 2016.

The Panel noted that the additional information was provided by, and concerned acts and omissions by, Astellas Europe. The Panel noted that Astellas Europe was not a member of the ABPI, although it was a member of EFPIA. Astellas UK was a member of the ABPI. The Panel had previously noted that Astellas UK was responsible for the acts/omissions of its affiliates that fell within the scope of the Code including its UK based European headquarters. The Panel had previously stated that, in its view, this remained the position even if the UK based European affiliate had responded directly to the complaint. In the present matter, the Panel noted that the position of Astellas UK remained as set out above. The Panel also noted that Astellas Europe, as a consequence of its membership of EFPIA, agreed to be bound by the UK Code including any applicable sanctions. This was set out in various EFPIA codes.

The Panel noted all the concerns and comments it had raised previously. It was appalled at the conduct of senior managers as revealed in the additional information in relation to the two cases and resulting audits. Senior managers failed to provide full and accurate details to the Panel, the Appeal Board and the Authority in relation to the audits. Some very important details, although hinted at by the Panel, the Appeal Board and by the Authority in the report of the audits, had only come properly to light as a result of the follow-up investigation ordered by Astellas Japan and carried out by an external counsel. This might, in part, have been triggered by the audits including the

conversation the PMCPA had with the CEO and President Astellas Group.

The report from external counsel stated that all those involved in compiling the information and drafting the response to Case AUTH/2747/1/15 were aware of the existence of the original selection criteria, as on 30 January 2015 senior employees' attention was drawn to the email which set out the original selection criteria. This was inconsistent with Astellas Europe's original response that material outside Zinc was not considered when drafting the response to the PMCPA.

The report from external counsel noted that the company's investigation following receipt of the second complaint (Case AUTH/2780/7/15) was inadequate. It failed to uncover the email of 26 October 2013 which stated that the commercial objective would be removed from the meeting agenda in order to 'smooth the passage' through Zinc but would remain an unwritten objective. The external counsel report noted that the failure to conduct a thorough fact-finding exercise at any time following the first PMCPA complaint was concerning and was even more troubling given the number of senior staff who knew exactly where to look for the relevant material.

The external counsel report stated that staff considered business concerns prevailed over compliance concerns and that there were no consequences for compliance breaches. Further, matters relating to the PMCPA investigation and the oncology business unit were kept within the management team and not shared with Japan. The concerns over integrity raised by the PMCPA in its report of the audits were amplified and confirmed by the external counsel findings.

The report from external counsel also acknowledged management failings and that the PMCPA criticisms of the Milan meeting were likely to apply to two other advisory board meetings which were described in the report as being similar. Mention was also made of the pressure of working in the business unit. Compliance concerns with regard to the Milan meeting were raised by the Nordic countries. The report by external counsel stated that the correction email (12 December 2013) was wholly inadequate to remedy the problems created by the promulgation of the original selection criteria.

The Panel considered that the additional information demonstrated that a number of individuals in Astellas Europe had not provided complete and accurate information. That this included very senior employees was extremely concerning. Astellas Europe's conduct was completely unacceptable. The report of the audits had found that there was an institutional failure with respect to compliance; a finding which, in the Panel's view, was now compounded by the additional information including the report by external counsel. The failings of Astellas Europe, as demonstrated by the additional information, went beyond, and were arguably even more serious than, those outlined in the report of the audits. The latest information demonstrated that Astellas Europe staff had lied about the original selection criteria on a number of occasions and not limited to Astellas Europe's response to the complaints but including when interviewed individually by members of the Authority at the audit, when they appeared before the Appeal Board in relation to the reports from the Panel in both cases and at the appeal in Case AUTH/2780/7/15. The failure to provide accurate, complete information at an audit and to the Appeal Board was a very serious matter. The truthfulness and accuracy of such comments and submissions to the Authority was fundamental to the integrity of self-regulation. It was remarkable that the individuals concerned had not provided the correct information sooner despite having had every opportunity to do so; the true position only emerged after those from the PMCPA carrying out the audits had spoken to the Japanese parent company and a report from external counsel was commissioned. The Panel was also concerned about the newly revealed breadth of compliance failures such as flawed processes including human resources processes wherein vital compliance material was not recognized as such, and the apparently unfettered influence of the named senior individuals upon matters such as disciplinary investigations. The Panel noted that very senior employees had left Astellas Europe. The Panel decided that it would report Astellas Europe to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to consider in relation to Paragraphs 11.3 and 11.4 of the Constitution and Procedure. Astellas UK would be advised accordingly.

**COMMENTS FROM ASTELLAS EUROPE AND ASTELLAS UK ON THE REPORT FROM THE PANEL**

At the consideration of the report the representatives from Astellas Europe sincerely apologised for the significant cultural and compliance failings created and caused by the actions and behaviours of some of its very senior managers. Globally Astellas viewed the current position as a corporate crisis. The newly appointed President of Astellas Europe referred to his global experience with the company and stressed his commitment to improve corporate culture such that ethics and compliance were embedded throughout the organisation. Some of that cultural change would come through the appointment of new people into key roles.

In addition to Astellas Europe's compliance action plan submitted as part of its response to the audit recommendations, the company submitted it was improving its corporate culture with new SOPs and whistle blowing arrangements. The company's compliance function would no longer be managed locally but would report to the newly appointed Senior Vice President and Head of Ethics and Compliance who in turn reported to the global company. Senior leadership in medical affairs now reported globally and was no longer managed by Europe. Dedicated compliance professionals would also be employed at every European affiliate.

In response to questions the Astellas Europe representatives explained that the main culprits had

left the company and further remaining members of staff were being given additional training. There had been adverse consequences for some staff at their annual appraisal. The new President of Astellas Europe was also currently acting as head of human resources (HR). A strong message had been given to the organisation about the seriousness of the situation. The seriousness of the situation had not previously been well communicated to Japan by Astellas Europe but following the PMCPA's interview of the Global CEO and President (as part of the December 2015 audits) immediate action was taken including an investigation undertaken with the assistance of external counsel.

The representatives from Astellas UK submitted that the company took its responsibilities under the Code very seriously. The UK General Manager reported to a position in the Netherlands which in turn reported to Astellas Europe. The UK company noted that very senior managers from Astellas Europe had colluded to deliberately mislead and not tell the truth. Such dishonesty was completely unexpected and was not at all known to the UK until it saw the report from external counsel which was provided as part of the report to the Appeal Board. The UK company was committed to working closer with Astellas Europe to clarify responsibilities and to ensure that the UK approved and certified any activity undertaken by its European affiliates that involved a UK health professional or took place in the UK. The company would also take responsibility for any future complaints under the Code about such activities. The UK company referred to ongoing compliance work including the seven work streams it had established to address findings from the audit.

[Post meeting note: Subsequently following the Appeal Board's consideration of the report in May 2016 Astellas stated that the internal investigation would have happened regardless of the PMCPA's interview of the Global CEO and President. The external counsel report, dated 24 March 2016 referred to an Astellas Europe Board resolution dated 20 January 2016 to investigate the matters described in the two cases including the PMCPA audit report].

**APPEAL BOARD CONSIDERATION OF THE REPORT FROM THE PANEL**

The Appeal Board welcomed the full apology made by the representatives of Astellas Europe at the consideration of the report, particularly as no apology was included in the papers for the case. However, the Appeal Board considered that such multiple organisational and cultural failings meant that this was one of the worst cases it had ever had to consider. As stated in the report of the audits there was an institutional failure with respect to compliance. Very senior staff had lied and there was deception on a grand scale. The Appeal Board was appalled and astonished that senior managers from Astellas Europe had made a concerted attempt to deceive it and the PMCPA. In that regard the Appeal Board considered the PMCPA's foresight to interview the Global CEO and President of Astellas Inc during the audit was pivotal in bringing these failings to light. It was a truly shocking state of affairs. The Appeal Board noted that these concerns did not relate to Astellas UK.

This was the third time Astellas Europe had been reported to the Appeal Board by the Panel and the second time Astellas UK had been reported to the Appeal Board by the Panel (including Case AUTH/2747/1/15).

The Appeal Board whilst recognising the difficulties of the situation, considered that Astellas UK should have attempted to exercise greater control on compliance matters in relation to the meeting at issue, the investigation of and response to the complaints and the Panel's reports to the Appeal Board. This was especially important given that Astellas UK was responsible for the acts/omission of its affiliates that fell within the scope of the Code including its UK based European headquarters. Given the information about the lies and deception, it was not surprising that Astellas Europe had asserted itself and taken the lead in responding to Cases AUTH/2747/1/15 and AUTH/2780/7/15.

The Appeal Board noted that Astellas Europe, as a member of EFPIA, was bound by the codes of EFPIA member associations including any applicable sanctions.

The Appeal Board considered that the integrity of self-regulation was reliant upon pharmaceutical companies providing complete and accurate information. The conduct of senior staff at Astellas Europe had been totally unacceptable and potentially harmful to self-regulation in this regard. It was also disappointing that Astellas UK had not taken firm action. There were multiple failings in these cases. The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure that both Astellas Europe and Astellas UK should again be publicly reprimanded for this failure.

The Appeal Board noted that the UK health professionals who attended the meeting had been provided with two corrective statements and case reports which, given the emergence of new information, gave a misleading account of the arrangements for the meeting at issue. This was wholly unacceptable. Consequently the Appeal Board decided, in accordance with Paragraph 11.3 of the Constitution and Procedure, to require Astellas Europe and Astellas UK to issue a fresh corrective statement to all the UK attendees at the meeting to clarify the position. This would be the third corrective statement. It should refer to both case reports. Under Paragraph 11.3 details, of the proposed content and mode and timing of dissemination of the corrective statement must be provided to the Appeal Board for approval prior to use. [The corrective statement appears at the end of the report.]

The Appeal Board also decided, given the seriousness of the failings, its concerns about the conduct of Astellas as set out above and the responsibility of Astellas UK for its parent company, to report Astellas Europe and Astellas UK to the ABPI Board. This was in accordance with Paragraph 12.1 of the Constitution and Procedure.

**ABPI BOARD CONSIDERATION OF THE REPORT FROM THE APPEAL BOARD**

The ABPI Board noted that breaches of Clauses 2, 9.1, 12.1, 18.1 and 20.1 of the Code had been ruled. The companies had been reported to the Appeal Board and both had been publicly reprimanded and required to issue corrective statements. The companies had been audited in December 2015 and were to be re-audited in September 2016.

The ABPI Board was extremely concerned at the multiple organisational and cultural failings at Astellas. There was an institutional failure. Very senior staff at Astellas Europe had lied and there was deception on a grand scale which was appalling and shocking.

The totally unacceptable behaviour of senior staff at Astellas Europe was potentially harmful to the integrity of self-regulation which relied upon companies providing complete and accurate information. The ABPI Board noted that Astellas UK was the member of the ABPI and that Astellas UK was responsible for the acts/omissions of affiliates that fell within the scope of the Code including its UK based European headquarters.

The ABPI Board decided that Astellas UK should be suspended from membership of the ABPI for a period of 12 months commencing 24 June. The ABPI Board also decided that it wanted sight of the reports of the September 2016 re-audits of Astellas UK and Astellas Europe so that it could review the position, including the length of the suspension, before the end of 2016. The re-audits must show demonstrable improvements at both companies particularly in relation to corporate culture.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in September 2016 and the report of the audits was considered by the Appeal Board in November.

The Appeal Board noted that although both companies had worked hard to implement the recommendations from the previous audits and to ensure compliance was truly embedded, there was still work to do.

With regard to Astellas Europe, the Appeal Board noted that the institutional failure with respect to compliance was starting to change. Both companies had, *inter alia*, issues with certification. The Appeal Board decided that both should be re-audited in April 2017 and on receipt of the report for those re-audits it would decide whether further sanctions were necessary.

**ABPI BOARD FURTHER REVIEW**

At its meeting in December 2016, the ABPI Board reviewed the progress made by both companies and the work still to be completed noting that it took time to change culture and to truly embed compliance. It noted the Appeal Board's decision that both companies should be re-audited in April 2017. Although the ABPI Board was encouraged by the improvements and progress made by both Astellas Europe and Astellas UK it decided that the suspension of Astellas UK from membership of the ABPI should continue. The ABPI Board would review the position in June 2017 after the re-audits.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in April 2017 and the report of the audits was considered by the Appeal Board in May 2017. The Appeal Board noted that Astellas UK and Astellas Europe were now working more closely and there was more open communication with staff. Both companies had been working to implement the recommendations of the previous audits and to ensure compliance was embedded. However, the Appeal Board noted the number of issues highlighted in the report and that there was still much work to be done.

The Appeal Board accepted that it took a long time to change culture but it was not convinced that progress was being made at an appropriate speed particularly given the issues that had come to light in Cases AUTH/2883/10/16, AUTH/2939/2/17 and AUTH/2940/2/17. This was particularly worrying given the level of scrutiny the companies were under. In the view of the Appeal Board, Astellas had much work still to do.

In relation to Case AUTH/2780/7/15 the Appeal Board decided that both companies should be re-audited in October 2017 at the same time as the audits required in Cases AUTH/2939/2/17 and AUTH/2940/2/17 and the re-audit in Case AUTH/2883/10/16 (Astellas UK only).

The Appeal Board noted the outcome of the audit in Case AUTH/2883/10/16 and the re-audits in Case AUTH/2780/7/15, the decisions to report Astellas UK to the ABPI Board in relation to Case AUTH/2883/10/16 and Astellas UK and Astellas Europe in relation to Cases AUTH/2939/2/17 and AUTH/2940/2/17. It also noted its concerns regarding the lamentable lack of concern for patient safety and wholly inadequate oversight and control. Whilst noting this was a matter for the ABPI Board, the Appeal Board's view was that Astellas UK was not ready to resume membership of the ABPI and the suspension should continue.

**ABPI BOARD FURTHER REVIEW**

At its meeting in June 2017 the ABPI Board agreed with the Appeal Board's comments and concerns about the re-audits in April 2017.

The ABPI Board noted and endorsed the Appeal Board's views about the total failure of the companies' systems in relation to the control of prescribing information, the lamentable lack of concern for patient safety, wholly inadequate oversight and control and initial lack of urgency. It was a woeful state of affairs.

The ABPI Board gave serious consideration to expelling Astellas UK from membership of the ABPI. However, it noted the commitments from

Astellas Europe, the global company and of the new UK General Manager. The companies had made voluntary admissions and it was now imperative that the October re-audits showed significant progress. The ABPI Board decided that it would extend the suspension of Astellas UK from membership of the ABPI for another 12 months. This further period would run uninterruptedly from the initial period of suspension and would then amount to the maximum suspension (two years) allowed under the ABPI Articles of Association.

The ABPI Board also decided that it wanted sight of the report of the October 2017 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of 2017. If the report of the re-audits did not show significant improvement and progress at both companies, then the ABPI Board would consider expelling Astellas UK from membership of the ABPI. The companies should consider undergoing an external assessment of progress, particularly in relation to risk management of compliance in the broadest sense, ie including matters beyond the scope of the Code, with the outcome to be available at the time of the October 2017 re-audits.

The ABPI Board also decided that the MHRA should be advised of the ABPI Board's very serious concerns about the conduct of Astellas UK and Astellas Europe particularly in relation to the matters concerning patient safety. EFPIA should also be updated and asked to ensure the EFPIA Board was informed of the position.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in October 2017 and the report of the re-audit was considered in November. The Appeal Board noted that as these were the fourth audits of the companies and given that Astellas UK was currently suspended from membership of the ABPI, it expected substantial progress and improvements from both companies. This expectation had not been met. The Appeal Board acknowledged that some progress had been made. The companies must take prompt action to implement the findings and recommendations in the report of the October 2017 re-audits.

The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been positive changes in the company culture. However, it was not convinced that the expected progress was being made, especially since the April 2017 re-audits.

Overall, the Appeal Board's view was that the rate of progress was inadequate and that the companies were not where they should be. There was still much work to do. The Appeal Board queried whether there was an element of structural inertia or perhaps fear of wrongdoing which was inhibiting or slowing the rate of progress.

Despite its criticisms, the Appeal Board noted the positive steps taken by the leadership of Astellas to engage more broadly with staff and drive changes.

The Appeal Board decided that both companies should be re-audited in April 2018. At which point it expected the 2018 global staff survey to demonstrate improvements at Astellas Europe and Astellas UK.

Whilst noting that this was entirely a matter for the ABPI Board, the Appeal Board's view was that if the report of the October 2017 re-audits and Astellas' response had come at the end of the two year suspension limit, then Astellas would have fallen well short of the standard required to resume membership of the ABPI. Unless substantial progress was seen in the report of the re-audits in April 2018, in the Appeal Board's view, Astellas UK would be at serious risk of a recommendation that it be expelled from membership of the ABPI.

**ABPI BOARD FURTHER CONSIDERATION**

The ABPI Board noted the Appeal Board's comments and concerns about the re-audits in October 2017 and the additional information provided by Astellas.

With regard to the external assessment of progress, particularly in relation to risk management of compliance in the broadest sense ie including matters beyond the scope of the Code, the ABPI Board noted the information provided by Astellas.

Following a change in tone from the top of Astellas, the ABPI Board recognised that meaningful progress had been made by the companies. The ABPI Board understood the difficulty inherent in making wide-sweeping cultural changes, and how long it took for those changes to become fully embedded within a large organisation. However, the ABPI Board acknowledged Astellas' clear commitment to further improvement.

The ABPI Board noted Astellas' statement that its materials were compliant in May 2017 in relation to issues of patient safety.

The ABPI Board also decided that it wanted sight of the report of the April 2018 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of the current suspension in June 2018.

The ABPI Board decided that taking all the circumstances into account it would take no further action at this stage in relation to the expulsion of Astellas from membership of the ABPI. The suspension from membership of the ABPI would remain in place until June 2018.

The ABPI Board also decided that the MHRA should be advised of the position. EFPIA should also be updated and asked to ensure that the EFPIA Board was informed of the position.

**APPEAL BOARD FURTHER CONSIDERATION**

In response to a request from the Appeal Board Astellas provided further information which showed that matters raised by the Appeal Board in November were being addressed more promptly than previously indicated.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in April 2018 and the report of the re-audits was considered in May 2018.

The Appeal Board noted the detailed responses from Astellas to the report of the April 2018 re-audits including that it was an accurate reflection of the work undertaken.

The Appeal Board noted the results of the 2018 staff survey and the progress made. Numerical increases had been shown in a number of parameters since the previous survey in July 2017. There were concerns about the comments made by staff. The Appeal Board also noted the differences in the Astellas UK results which were generally better than the Astellas Europe results. The Appeal Board considered that the Astellas Europe management committee scores although improved were still not where they should be.

The Appeal Board noted the comments in the report of the April 2018 re-audits and considered that both the leadership of Astellas Europe and Astellas UK had engaged with staff to bring about progress. There was still work to be done. The Appeal Board noted one of the recommendations was that members of the leadership team at Astellas Europe should be held to account and be challenged on compliance matters.

The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been further positive changes in the company culture and this needed to be continued. The Appeal Board noted that there had been some positive compliance initiatives. The discussion fora and communications continued and progress had been made including ensuring staff had time to complete training.

The Appeal Board noted that whilst as a percentage there had been a significant increase in the number of job bags, the overall number was still low. As Astellas increased its activities it must remain extremely vigilant to compliance requirements in particular in relation to certain higher risk activities such as patient support programmes, product launches etc. The true test of the compliance framework in Astellas and its approach would be when activity levels including higher risk activities were increased and the company was operating at business as usual.

The Appeal Board considered that, at long last, the re-audits in April 2018 showed that progress had been made and that the companies were building on momentum started in summer 2017.

The Appeal Board was concerned that these were the fifth audits of each company and that the first audits were in December 2015. It was extraordinary that it had taken so long to demonstrate meaningful change. The overall impression from the report of the April 2018 re-audits was that Astellas was showing improvement and momentum. However, whilst the companies had reached a certain level, given all the circumstances including that Astellas UK had been suspended from membership of the ABPI and that the Appeal Board still had concerns, the Appeal Board decided that Astellas Europe and Astellas UK should each be re-audited at the end of the first quarter of 2019 to ensure that the improvements and the momentum continued and were built upon.

On the information before it, and noting that Astellas UK was still to respond to the PMCPA in relation to matters raised following completion of the consideration of a complaint concerning Astellas UK, Case AUTH/2984/10/17, the Appeal Board decided that sufficient progress had been made by the companies such that the Appeal Board did not consider that it warranted a recommendation for the expulsion of Astellas UK from membership of the ABPI when the matter came before the ABPI Board on 5 June 2018.

**ABPI BOARD FUTHER CONSIDERATION**

In June 2018 the ABPI Board noted the comments from both the Appeal Board and Astellas.

The ABPI Board noted the limited information provided about matters raised in Case AUTH/2984/10/17. This was still to be considered by the PMCPA and the Appeal Board and was not before the ABPI Board for consideration.

The view of the Appeal Board was clear. The ABPI Board agreed with the Appeal Board's views and assessment of the re-audits and concluded that meaningful progress had now been made.

The ABPI Board believed that the culture in the companies had improved and noted that much of this had been led by the General Manager of Astellas UK. However, the Board recognised the importance of an ongoing commitment to ensure sustained culture change. On reviewing all the material, the ABPI Board had concerns about the sustainability of the changes made given that there had already been five audits/re-audits, and especially as further types of activity were still to be fully re-introduced across the companies.

The ABPI Board therefore decided that it wanted to see the report of the 2019 re-audits and be informed of major developments including the outcome of Case AUTH/2984/10/17.

In the circumstances, there was no need for the ABPI Board to consider expelling Astellas UK from membership of the ABPI. The suspension would end on 24 June 2018 and Astellas would revert to full membership of the ABPI.

Astellas should be cognisant of this ongoing sustainability requirement and monitoring (particularly in light of the matters still to be concluded in Case AUTH/2984/10/17) when communicating about the Board's decision.

The ABPI Board also decided that the MHRA should be advised of the position and that EFPIA should be updated and asked to ensure that the EFPIA Board was informed of the position.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in April 2019 and the report of the re-audits was considered in May 2019.

The Appeal Board noted the detailed response from Astellas Europe and Astellas UK to the report of the April 2019 re-audits.
The Appeal Board noted two new senior appointments; a new President EMEA Operations who joined Astellas in July 2018 and a new General Manager, Astellas UK who was appointed from April 2019.

The Appeal Board noted from the report of the April 2019 re-audits that it appeared that a more compliant culture was embedded within Astellas with improved communication. It was essential that this was maintained.

The Appeal Board considered that Astellas UK must ensure a proper professional approach to investigating and responding to any complaint under the Code such that the shortcomings in Case AUTH/2984/10/17 were not repeated. The Appeal Board noted that an audit had not been required in Case AUTH/2984/10/17. The case had, in accordance with established practice, been discussed as part of an examination of the company's culture at the re-audits.

The Appeal Board noted that these were the sixth audits/re-audits of each company and that the first audits were in December 2015. The Appeal Board considered that, on the information provided in the report of the April 2019 re-audits, it appeared that the companies had made further improvements, that this would be maintained and broadly the companies were where they should be. The Appeal Board, however, remained very concerned about the amount of time it had taken Astellas to reach this point. The Appeal Board noted that Astellas stated that it would follow up on the issues identified in the report of the April 2019 re-audits and it was committed to maintaining its approach to embedding a sustainable compliance culture. The Appeal Board noted a number of activities/actions were due to be undertaken. On the understanding that this work was completed, that the progress shown to date was continued and a company-wide commitment to compliance was maintained, the Appeal Board decided that, on the basis of the information in the report of April 2019 re-audits, no further action was required in relation to Case AUTH/2780/7/15, Case AUTH/2883/10/16, Cases AUTH/2939/2/17 and AUTH/2940/2/17.

The Appeal Board noted that the audit/re-audits in these four cases had been required by the Appeal Board. They had not been required by the ABPI Board. Nonetheless, the Appeal Board noted the ABPI Board's request to see the report of the April 2019 re-audits.

At the re-audits in April 2019 it was noted that the MHRA decided that Astellas advertising materials should be submitted for review. This was introduced for all new materials issued since 1 December 2018.

**ABPI BOARD UPDATE**

In June 2019 the ABPI Board received an update as requested. It noted the comments from both the Appeal Board and Astellas and the improvements made.

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| **Complaint received** | **8 July 2015** |
| **Undertaking received** | **5 November 2015** |
| **Appeal Board consideration** | **15 October 2015, 21 January 2016, 25 February, 28 April, 11 November, 25 May 2017, 16 November, 7 December, 17 May 2018, 22 May 2019** |
| **ABPI Board consideration** | **7 June 2016, 6 December 2016, 6 June 2017, 5 December, 5 June 2018** |
| **ABPI Board update** | **4 June 2019** |
| **First corrective statement was required in Case AUTH/2747/1/15 and issued on 1 July 2015** | |
| **Second corrective statement issued** | **4 January 2016** |
| **Panel reconvened** | **6 April 2016** |
| **Third corrective statement issued** | **28 June 2016** |
| **Interim case report first published** | **15 December 2015** |
| **Case completed** | **22 May 2019** |

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Astellas Pharma Europe and Astellas UK sent copies of the case report and the company's corrective statement to all UK attendees at the meeting. The materials were sent on 4 January 2016.

Astellas Pharma Europe Ltd was required to provide UK delegates who attended its meeting on 27/28 February 2014 with a corrective statement. The meeting (Case AUTH/2747/1/15 was ruled in breach of the ABPI Code of Practice for the Pharmaceutical Industry and the corrective statement was sent on 1 July 2015.

Following a second complaint Case AUTH/2780/7/15), the Code of Practice Panel ruled that Astellas Pharma Europe and Astellas UK had provided the Panel and the Appeal Board with false and incomplete information regarding the selection criteria for attendees at the meeting. High standards had not been maintained and this had brought discredit upon, and reduced confidence in, the pharmaceutical industry.

As a result Astellas Pharma Europe and Astellas UK have been required to issue this further corrective statement and to circulate a copy of the published report for Case AUTH/2780/7/15 which contains full details and is enclosed.

Details of these cases (Case AUTH/2747/1/15 and Case AUTH/2780/7/15) are also available on the PMCPA website (www.pmcpa.org.uk).

Astellas Europe and Astellas UK sent copies of the case report and the company's corrective statement to all UK attendees at the meeting. The materials were sent in on 28 June 2016.

'Corrective Statement

Astellas Pharma Europe and Astellas UK have already sent corrective statements with regard to the meeting you attended in Milan on 27/28 February 2014.

Following a complaint under the ABPI Code of Practice for the Pharmaceutical Industry (Case AUTH/2747/1/15) breaches of the Code were ruled and the Code of Practice Panel reported Astellas Pharma Europe to the Code of Practice Appeal Board which required the company to issue a corrective statement. This was sent to you on 1 July 2015.

A subsequent complaint (Case AUTH/2780/7/15) revealed that the information provided in Case AUTH/2747/1/15 about the selection criteria for attendees at the meeting had been false and incomplete. The Panel reported Astellas Pharma Europe and Astellas UK to the Appeal Board which required a further corrective statement to be issued. This was sent to you on 4 January 2016.

Following the provision of further information from Astellas Pharma Europe which showed the extent to which the Panel and the Appeal Board had been misled and the seniority of the personnel involved, the Panel again reported Astellas Pharma Europe and Astellas UK to the Appeal Board. As a result Astellas Pharma Europe and Astellas UK have been required as part of a number of sanctions to issue another corrective statement and to circulate a copy of the updated report for Case AUTH/2780/7/15 which contains full details.

Details of these cases (Case AUTH/2747/1/15 and Case AUTH/2780/7/15) which include details of the subsequent suspension of Astellas UK from membership of the ABPI are also available on the PMCPA website (www.pmcpa.org.uk).'

**CASE AUTH/2883/10/16**

# VOLUNTARY ADMISSION BY ASTELLAS UK

## Patient support programmes

**Astellas UK voluntarily admitted breaches of the Code with regard to patient support programmes and the conduct of a third party agency. The patient support programmes, Fresh Start and VIP related to Betmiga (mirabegron) and Vesicare (solifenacin succinate) respectively. Both medicines were for the symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as might occur in patients with overactive bladder syndrome.**

**As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Astellas UK.**

**Astellas explained that on 22 September 2016 a member of staff searched Google for the Betmiga patient support programme (Fresh Start), and found patient support materials for Vesicare and Betmiga clearly displayed on the website of one of Astellas's agencies. The Betmiga material was certified on 3 April 2014, first used on 12 May 2014 and withdrawn on 4 April 2016. The Vesicare material was certified on 28 September 2015. The certified method of dissemination for the material incorrectly identified health professionals including via representatives.**

**Astellas understood that in displaying the material (without Astellas's permission), the agency's intention was to market its abilities, driven by a new creative director who was not trained on the Code. Astellas immediately asked the agency to remove the material which it did. The webpage went live on 15 April 2016 and was taken down on 22 September 2016.**

**Astellas discovered that the agency had also used imagery from another Astellas programme which was closed on 22 May 2016 (Remind Me). This imagery was displayed from 15 April 2016 until 22 September 2016. This identified Astellas medicines within the transplantation area and included product brand names and a claim.**

**Astellas considered that the use of the brand names and therapeutic indications on the agency website went beyond any requirement to market creative capabilities and constituted promotion of prescription only medicines to the public, in breach of the Code. In addition, given the seriousness of this, Astellas UK understood that the Panel might wish to consider the requirements of other clauses including Clause 2.**

**The detailed response from Astellas UK appears below.**

**The Panel noted that an Astellas employee had found patient support materials for Betmiga and Vesicare on the agency's website after he/she had specifically searched the internet for the Betmiga patient support programme (Fresh Start). Having discovered the Betmiga and the Vesicare materials on the agency website, Astellas then found material from the Remind Me programme which supported patients taking Prograf (tacrolimus) or Advagraf (tacrolimus SR) for the prophylaxis of transplant rejection. None of the material had been posted on the agency's website with Astellas's knowledge or permission.**

**The Panel noted that the material shown on the website for Betmiga and Vesicare consisted of the front page of two patient support booklets aimed at those taking one or the other medicines. From the text below, which detailed the client, the brief and the solution, it was clear that both medicines were for the treatment of overactive bladder. The material shown for the Remind Me programme was the nurse guide.**

**On balance, despite medicines and their indication appearing on an open access website, the Panel did not consider that medicines had been promoted to the public; the website was not aimed at the public *per se*. The company had not failed to maintain high standards. No breaches of the Code were ruled including Clause 2.**

**Astellas noted that until the events described above, it had run the two patient support programmes; VIP, for all patients prescribed Vesicare and Fresh Start, for those prescribed Betmiga. The third party agency was engaged to develop material and to run the support programmes via its team of nurses who manned a patient support line. Both patient support programmes had now been terminated due to Astellas's concern in relation to its lack of oversight and support as detailed below.**

**When the programmes started in 2006 (VIP) and 2013 (Fresh Start) the nurses on the patient support line were trained face-to-face by Astellas on the relevant summaries of product characteristics (SPCs) as well as on adverse event reporting. In addition, nurses were given a 'script' to aid their discussions with patients. Although the adverse event training was repeated once a year via an Astellas pharmacovigilance training slide deck, there was no record of any further training on Vesicare or Betmiga despite the SPCs having changed a number of times in intervening years. Although Astellas had not provided revised SPCs to the third party agency, it had confirmed that if nurses needed to refer to an SPC it would always be viewed online via the electronic medicines compendium (eMC) website to provide the latest information.**

**Although Astellas had monitored the number of patients enrolled into each patient support programme monthly and had continued to pay the agency the monthly fixed fee, it had not provided similar ongoing oversight and support for the nurse helpline in relation to product training. Whilst Astellas recognised that these programmes should have had ongoing consistent oversight, they had been managed by a series of colleagues without appropriate handover or training.**

**Astellas considered that, given that the nurses interacted directly with patients, this was a failure to maintain high standards. Astellas also understood that the Panel might wish to consider the requirements of Clause 2 in relation to the lack of oversight and supervision.**

**Astellas submitted that because of errors in setting up job bags in Zinc, some materials from both programmes had gone past the two year period without being re-certified. All of the VIP material including that withdrawn in March 2014 had been reviewed and Astellas considered that the content was still appropriate for use; however, the job bags had been very poorly set up including incorrect audience, poor information on objectives and having been initiated as a promotional item. With regard to Fresh Start, materials were identified in April 2016 that still described Betmiga as 'new' having been previously re-certified in April 2014. The word 'new' should have been removed from this material by February 2014. Other items had been withdrawn in error but remained active. In addition Astellas was concerned that the frequently asked questions section of the nurses' script (certified on 21 July 2015) no longer accurately reflected all adverse events listed in the current SPC (nausea was omitted). In addition, the Betmiga SPC was updated in April 2016 and the nurses' script was not revised to reflect the addition of a number of common side effects (constipation, diarrhoea, headache and dizziness). Astellas thus considered that the nurses' script was inaccurate and did not reflect the available evidence in relation to side effects. In addition, this amounted to a failure to maintain high standards and had the potential to impact on patient safety, which would be contrary to the requirements of Clause 2.**

**Astellas submitted that the errors noted above with regard to the use of Zinc may have been due to human error and that human error was attributable to the omission in the Fresh Start nurses script.**

**Astellas considered that, given that the materials at issue were distributed to patients, this amounted to a failure to maintain high standards. Astellas understood that the Panel might wish to consider the requirements of Clause 2 in relation to this lack of oversight and supervision.**

**In addition, Astellas found out in August 2016 that the third party agency had been sending a survey to patients after 3 months on either programme. This patient feedback information was previously provided to Astellas and outcomes from the questionnaire used in a promotional piece of material in 2009. The agency was instructed to discontinue this activity immediately.**

**The Panel noted that Astellas's oversight of the agency nurses who delivered the two patient support programmes was extremely poor. Although when both programmes first started, the nurses who were to man the helplines were trained on the relevant medicine (Betmiga or Vesicare), they received no further product specific training despite the fact that the SPCs for both products had since changed a number of times; some of those changes related to changes to Section 4.8, Undesirable effects. Further the telephone scripts which they had initially been given had not been revised; the script for the VIP helpline was dated October 2012. The script for the Fresh Start programme was dated March 2013 and did not reflect the addition to the Betmiga SPC of a number of common side effects (constipation, diarrhoea, headache and dizziness). Both scripts were thus inaccurate and out-of-date and the Panel ruled breaches of the Code. The Fresh Start script did not accurately reflect up-to-date information on possible side effects and in that regard the Panel ruled a breach of the Code. The Panel noted Astellas's submission that if nurses were asked questions about Betmiga or Vesicare that needed reference to the SPC, they would access the eMC website for the latest version. The nurses received annual training on adverse event reporting. It was unclear whether this had been updated annually. It was also unclear why training on other matters outlined above had not been provided. Overall the Panel considered that such inadequate training of those who were expected to interact directly with patients was wholly unacceptable. High standards had not been maintained in breach of the Code. The Panel further considered that the failure to properly train the nurses and keep them updated with product changes was such as to bring discredit upon and reduce confidence in the pharmaceutical industry. It was crucial that out of all of the options available, patients could rely completely upon the industry for up-to-date and accurate information about their medicines. A breach of Clause 2 was ruled.**

**In addition Astellas's oversight of the patient support materials was very poor. In that regard the Panel noted Astellas's submission that materials had been set up wrongly in Zinc such that although they were withdrawn in Zinc, mostly in 2014, they continued to be used by the agency beyond two years without being re-certified. The Panel ruled a breach of the Code.**

**Betmiga material which described the medicine as 'new' for more than one year was ruled in breach including that high standards had not been maintained.**

**The Panel noted Astellas's submission that not all the patient materials were certified in a hard copy final form before use and those that were, were signed by a brand manager and not a nominated signatory. Further, the Panel noted that the patient satisfaction surveys had not been certified at all. Breaches of the Code were ruled including that high**

**standards had not been maintained. No breach was ruled in relation to certification of promotional materials.**

**The Panel noted the number of materials which had not been correctly processed for certification. In that regard the Panel considered that Astellas's lack of control of material was such as to bring discredit upon, and reduce confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.**

**During its investigation into the issues noted above, Astellas found out that the nurses manning the patient support lines still also worked for the NHS. This was not previously known, and Astellas considered that this additional information meant that the agency fitted the definition of an institution, organisation or association of health professionals and transfers of value in relation to services provided on behalf of a company were required to be disclosed. This disclosure had not taken place for transfers of value made in 2015. Additionally, payments made to pharmacies in relation to enrolment of patients onto the Fresh Start programme had not been disclosed. The company stated it was addressing this and would upload the relevant data to the ABPI central platform as soon as possible.**

**The Panel noted that the nurses who manned the patient helplines had been supplied by the agency. Astellas did not know how much of the fee it had paid the agency had gone either to the nurses as a group or to each individual nurse. At the start of the patient support programmes, Astellas had known who the nurses were through face-to-face training for the VIP programme (2006) and the Fresh Start programme (2013).**

**The Panel noted that the Code required companies to declare transfers of value made directly or indirectly to health professionals and healthcare organisations located in Europe. The definition of healthcare organization included 'an organization through which one or more health professional or other relevant decision makers provide services'. In that regard, the Panel considered that although creative agencies would not normally be considered healthcare organisations, in this case the nurses on the patient helplines had provided their services through the agency. In that regard the Panel considered that Astellas must declare the amount paid to the agency for the nurses on the ABPI central platform. If the company became aware of the individual identity of the nurses then the amount paid should be declared for each individual. It was unacceptable that the contract with the agency did not appear to be such that the company could identify the amount(s) paid. The Panel further noted that monies paid to pharmacies in relation to the enrolment of patients into the Fresh Start programme had not been declared. Breaches of the Code were ruled.**

**The Panel was extremely concerned about is rulings and comments above. Some of the matters raised went to the heart of self-regulation and patient safety. The company's oversight of the patient support programmes at issue had been lamentable.**

**Notwithstanding the fact that Astellas UK was currently suspended from membership of the ABPI and already undergoing a series of audits of its procedures under the Code, the Panel decided, in accordance with Paragraph 8.2 of the Constitution and Procedure, to report the company to the Appeal Board for it to consider whether further sanctions were appropriate in this case.**

**The detailed comments from Astellas UK on the report from the Panel appear below.**

**The Appeal Board noted that this case had arisen from a voluntary admission by Astellas UK and the company had accepted all breaches of the Code including Clause 2. The Appeal Board also noted that Astellas UK had made a sincere apology for its failings in this case.**

**The Appeal Board considered that this case raised serious concerns about multiple failings and a complete lack of control in Astellas UK's review and certification process which was entirely unacceptable.**

**The Appeal Board was very concerned to note that Astellas UK had little or no knowledge about the qualifications of the nurses employed by its agency or of what they did or said to patients. Astellas should have had far greater oversight including feedback and audit of the nurses' interactions with patients. It was an appalling failure in particular that the nurses were not trained or updated on changes to the relevant SPCs. It was essential that patients could rely completely upon the industry for up-to-date and accurate information about medicines. The Appeal Board considered that the deplorable failure of process and oversight in this case raised serious concerns with regard to patient safety and public confidence in the pharmaceutical industry.**

**The Appeal Board noted that as a consequence of Case AUTH/2780/7/15 Astellas UK was currently suspended from membership of the ABPI. Astellas UK and Astellas Pharma Europe had each been audited twice (December 2015 and September 2016) and each would be audited again in April 2017.**

**The Appeal Board was minded to report Astellas UK to the ABPI Board but given the exceptional circumstances, including that the re-audits in Case AUTH/2780/7/15 were due to be carried out very shortly, it decided that the issues that had arisen in this case should be looked at as part of the upcoming re-audit of Astellas UK, including examination of patient support programmes and certification of material. On consideration of the report of the re-audits the Appeal Board would reserve its decision on whether to report Astellas UK to the ABPI Board.**

**The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, Astellas UK should be publicly reprimanded for a lamentable lack of concern for patient safety and wholly unsatisfactory oversight and control of the patient support programmes and of the nurses employed to deliver them.**

**Astellas UK and Astellas Europe were re-audited in April 2017 and the report was considered by the Appeal Board in May 2017.**

**The Appeal Board noted that Astellas UK and Astellas Europe were now working more closely and there was more open communication with staff. Both companies had been working to implement the recommendations of the previous audits and to ensure compliance was embedded. However, the Appeal Board noted the number of issues highlighted in the report and that there was still much work to be done.**

**The Appeal Board accepted that it took a long time to change culture but it was not convinced that progress was being made at an appropriate speed particularly given the issues that had come to light in Cases AUTH/2883/10/16, AUTH/2939/2/17 and AUTH/2940/2/17. This was particularly worrying given the level of scrutiny the companies were under. In the view of the Appeal Board, Astellas had much work still to do.**

**In relation to Case AUTH/2883/10/16 the Appeal Board decided that Astellas UK should be re-audited in October 2017 at the same time as the re-audit required in Case AUTH/2780/7/15 and the audit required in Cases AUTH/2939/2/17 and AUTH/2940/2/17 in relation to both Astellas UK and Astellas Europe.**

**In relation to Case AUTH/2883/10/16 the Appeal Board noted that it had reserved its position in relation to additional sanctions in this case until it had seen the report of the April 2017 re-audits. Bearing in mind that the case related to patient safety and a lack of control and oversight, the Appeal Board decided that in accordance with Paragraph 12.1 of the Constitution and Procedure, Astellas UK should be reported to the ABPI Board.**

**The Appeal Board noted the outcome of the audit in Case AUTH/2883/10/16, and the re-audits in Case AUTH/2780/7/15, the decisions to report Astellas UK to the ABPI Board in Cases AUTH/2883/10/16, AUTH/2939/2/17 and AUTH/2940/2/17 in relation to both Astellas UK and Astellas Europe. It also noted its concerns regarding the lamentable lack of concern for patient safety and wholly inadequate oversight and control. Whilst noting this was a matter for the ABPI Board, the Appeal Board's view was that Astellas UK was not ready to resume membership of the ABPI and the suspension should continue.**

**The ABPI Board noted the rulings of breaches of the Code, the decisions of the Appeal Board regarding audit, re-audit and the public reprimand.**

**The ABPI Board agreed with the Appeal Board's comments and concerns about the re-audits in April 2017.**

**The ABPI Board noted and endorsed the Appeal Board's views about the total failure of the companies' systems in relation to the control of prescribing information, the lamentable lack of concern for patient safety, wholly inadequate oversight and control and initial lack of urgency. It was a woeful state of affairs.**

**The ABPI Board gave serious consideration to expelling Astellas UK from membership of the ABPI. However, it noted the commitments from Astellas Europe, the global company and of the new UK General Manager. The companies had made voluntary admissions and it was now imperative that the October re-audits showed significant progress.**

**The ABPI Board decided that it would extend the suspension of Astellas UK from membership of the ABPI for another 12 months. This further period would run uninterruptedly from the initial period of suspension and would then amount to the maximum suspension (two years) allowed under the ABPI Articles of Association.**

**The ABPI Board also decided that it wanted sight of the report of the October 2017 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of 2017. If the report of the re-audits did not show significant improvement and progress at both companies, then the ABPI Board would consider expelling Astellas UK from membership of the ABPI. The companies should consider undergoing an external assessment of progress, particularly in relation to risk management of compliance in the broadest sense, ie including matters beyond the scope of the Code, with the outcome to be available at the time of the October 2017 re-audits.**

**The ABPI Board also decided that the MHRA should be advised of the ABPI Board's very serious concerns about the conduct of Astellas UK and Astellas Europe particularly in relation to the matters concerning patient safety. EFPIA should also be updated and asked to ensure the EFPIA Board was informed of the position.**

**Astellas UK and Astellas Europe were re-audited in October 2017 and the report of the re-audit was considered in November. The Appeal Board noted that as these were the fourth audits of the companies and given that Astellas UK was currently suspended from membership of the ABPI, it expected substantial progress and improvements from both companies. This expectation had not been met. The Appeal Board acknowledged that some progress had been made. The companies must take prompt action to implement the findings and recommendations in the report of the October 2017 re-audits.**

**The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been positive changes in the company culture. However, it was not convinced that the expected progress was being made, especially since the April 2017 re-audits.**

**Overall, the Appeal Board's view was that the rate of progress was inadequate and that the companies were not where they should be. There was still**

**much work to do. The Appeal Board queried whether there was an element of structural inertia or perhaps fear of wrongdoing which was inhibiting or slowing the rate of progress.**

**Despite its criticisms, the Appeal Board noted the positive steps taken by the leadership of Astellas to engage more broadly with staff and drive changes.**

**The Appeal Board decided that both companies should be re-audited in April 2018. At which point it expected the 2018 global staff survey to demonstrate improvements at Astellas Europe and Astellas UK.**

**Whilst noting that this was entirely a matter for the ABPI Board, the Appeal Board's view was that if the report of the October 2017 re-audits and Astellas' response had come at the end of the two year suspension limit, then Astellas would have fallen well short of the standard required to resume membership of the ABPI. Unless substantial progress was seen in the report of the re-audits in April 2018, in the Appeal Board's view, Astellas UK would be at serious risk of a recommendation that it be expelled from membership of the ABPI.**

**The ABPI Board noted the Appeal Board's comments and concerns about the re-audits in October 2017 and the additional information provided by Astellas.**

**With regard to the external assessment of progress, particularly in relation to risk management of compliance in the broadest sense ie including matters beyond the scope of the Code, the ABPI Board noted the information provided by Astellas.**

**Following a change in tone from the top of Astellas, the ABPI Board recognised that meaningful progress had been made by the companies. The ABPI Board understood the difficulty inherent in making wide-sweeping cultural changes, and how long it took for those changes to become fully embedded within a large organisation. However, the ABPI Board acknowledged Astellas' clear commitment to further improvement.**

**The ABPI Board noted Astellas' statement that its materials were compliant in May 2017 in relation to issues of patient safety.**

**The ABPI Board also decided that it wanted sight of the report of the April 2018 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of the current suspension in June 2018.**

**The ABPI Board decided that taking all the circumstances into account it would take no further action at this stage in relation to the expulsion of Astellas from membership of the ABPI. The suspension from membership of the ABPI would remain in place until June 2018.**

**The ABPI Board also decided that the MHRA should be advised of the position. EFPIA should also be updated and asked to ensure that the EFPIA Board was informed of the position.**

**Astellas UK and Astellas Europe were re-audited in April 2018 and the report of the re-audits was considered in May 2018.**

**The Appeal Board noted the detailed responses from Astellas to the report of the April 2018 re-audits including that it was an accurate reflection of the work undertaken.**

**The Appeal Board noted the results of the 2018 staff survey and the progress made. Numerical increases had been shown in a number of parameters since the previous survey in July 2017. There were concerns about the comments made by staff. The Appeal Board also noted the differences in the Astellas UK results which were generally better than the Astellas Europe results. The Appeal Board considered that the Astellas Europe management committee scores although improved were still not where they should be.**

**The Appeal Board noted the comments in the report of the April 2018 re-audits and considered that both the leadership of Astellas Europe and Astellas UK had engaged with staff to bring about progress. There was still work to be done. The Appeal Board noted one of the recommendations was that members of the leadership team at Astellas Europe should be held to account and be challenged on compliance matters.**

**The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been further positive changes in the company culture and this needed to be continued. The Appeal Board noted that there had been some positive compliance initiatives. The discussion fora and communications continued and progress had been made including ensuring staff had time to complete training.**

**The Appeal Board noted that whilst as a percentage there had been a significant increase in the number of job bags, the overall number was still low. As Astellas increased its activities it must remain extremely vigilant to compliance requirements in particular in relation to certain higher risk activities such as patient support programmes, product launches etc. The true test of the compliance framework in Astellas and its approach would be when activity levels including higher risk activities were increased and the company was operating at business as usual.**

**The Appeal Board considered that, at long last, the re-audits in April 2018 showed that progress had been made and that the companies were building on momentum started in summer 2017. The Appeal Board was concerned that these were the fifth audits of each company and that the first audits were in December 2015. It was extraordinary that it had taken so long to demonstrate meaningful change. The overall impression from the report of the April 2018 re-audits was that Astellas was showing improvement and momentum. However, whilst the companies had reached a certain level, given all the circumstances including that Astellas UK had been suspended from membership of the**

**ABPI and that the Appeal Board still had concerns, the Appeal Board decided that Astellas Europe and Astellas UK should each be re-audited at the end of the first quarter of 2019 to ensure that the improvements and the momentum continued and were built upon.**

**On the information before it, and noting that Astellas UK was still to respond to the PMCPA in relation to matters raised following completion of the consideration of a complaint concerning Astellas UK, Case AUTH/2984/10/17, the Appeal Board decided that sufficient progress had been made by the companies such that the Appeal Board did not consider that it warranted a recommendation for the expulsion of Astellas UK from membership of the ABPI when the matter came before the ABPI Board on 5 June 2018.**

**In June 2018 the ABPI Board noted the comments from both the Appeal Board and Astellas.**

**The ABPI Board noted the limited information provided about matters raised in Case AUTH/2984/10/17. This was still to be considered by the PMCPA and the Appeal Board and was not before the ABPI Board for consideration.**

**The view of the Appeal Board was clear. The ABPI Board agreed with the Appeal Board's views and assessment of the re-audits and concluded that meaningful progress had now been made.**

**The ABPI Board believed that the culture in the companies had improved and noted that much of this had been led by the General Manager of Astellas UK. However, the Board recognised the importance of an ongoing commitment to ensure sustained culture change. On reviewing all the material, the ABPI Board had concerns about the sustainability of the changes made given that there had already been five audits/re-audits, and especially as further types of activity were still to be fully re-introduced across the companies.**

**The ABPI Board therefore decided that it wanted to see the report of the 2019 re-audits and be informed of major developments including the outcome of Case AUTH/2984/10/17.**

**In the circumstances, there was no need for the ABPI Board to consider expelling Astellas UK from membership of the ABPI. The suspension would end on 24 June 2018 and Astellas would revert to full membership of the ABPI.**

**The ABPI Board also decided that the MHRA should be advised of the position and that EFPIA should be updated and asked to ensure that the EFPIA Board was informed of the position.**

**Astellas UK and Astellas Europe were re-audited in April 2019 and the report of the re-audits was considered in May 2019.**

**The Appeal Board noted the detailed response from Astellas Europe and Astellas UK to the report of the April 2019 re-audits.**

**The Appeal Board noted two new senior appointments; a new President EMEA Operations who joined Astellas in July 2018 and a new General Manager, Astellas UK who was appointed from April 2019.**

**The Appeal Board noted from the report of the April 2019 re-audits that it appeared that a more compliant culture was embedded within Astellas with improved communication. It was essential that this was maintained.**

**The Appeal Board considered that Astellas UK must ensure a proper professional approach to investigating and responding to any complaint under the Code such that the shortcomings in Case AUTH/2984/10/17 were not repeated. The Appeal Board noted that an audit had not been required in Case AUTH/2984/10/17. The case had, in accordance with established practice, been discussed as part of an examination of the company's culture at the re-audits.**

**The Appeal Board noted that these were the sixth audits/re-audits of each company and that the first audits were in December 2015. The Appeal Board considered that, on the information provided in the report of the April 2019 re-audits, it appeared that the companies had made further improvements, that this would be maintained and broadly the companies were where they should be. The Appeal Board, however, remained very concerned about the amount of time it had taken Astellas to reach this point. The Appeal Board noted that Astellas stated that it would follow up on the issues identified in the report of the April 2019 re-audits and it was committed to maintaining its approach to embedding a sustainable compliance culture. The Appeal Board noted a number of activities/actions were due to be undertaken. On the understanding that this work was completed, that the progress shown to date was continued and a company-wide commitment to compliance was maintained, the Appeal Board decided that, on the basis of the information in the report of April 2019 re-audits, no further action was required in relation to Case AUTH/2780/7/15, Case AUTH/2883/10/16, Cases AUTH/2939/2/17 and AUTH/2940/2/17.**

**The Appeal Board noted that the audit/re-audits in these four cases had been required by the Appeal Board. They had not been required by the ABPI Board. Nonetheless, the Appeal Board noted the ABPI Board's request to see the report of the April 2019 re-audits.**

**At the re-audits in April 2019 it was noted that the MHRA decided that Astellas advertising materials should be submitted for review. This was introduced for all new materials issued since 1 December 2018.**

**In June 2019 the ABPI Board received an update as requested. It noted the comments from both the Appeal Board and Astellas and the improvements made.**

**Astellas UK voluntarily admitted breaches of the Code with regard to patient support programmes and the conduct of a third party agency. The patient**

**support programmes, Fresh Start and VIP related to Betmiga (mirabegron) and Vesicare (solifenacin succinate) respectively. Both medicines were for the symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as might occur in patients with overactive bladder syndrome.**

**In addition to the clauses cited by Astellas, the Authority also asked the company to consider the requirements of Clauses 14.1 and 14.3 and noted that the materials might be covered by previous versions of the Code.**

**1 Actions of an Astellas's agency**

**VOLUNTARY ADMISSION**

Astellas UK explained that on 22 September 2016 a member of its medical team searched for the URL for the Betmiga patient support programme (Fresh Start), and found a page on the website of one of Astellas's third party agencies which clearly displayed a number of patient support materials for Vesicare and Betmiga. The Betmiga material, developed by the agency and certified by Astellas on 3 April 2014, was first used on 12 May 2014 and withdrawn on 4 April 2016; the agency was notified of such by email. The Vesicare material was certified on 28 September 2015. The materials were for patients prescribed either Betmiga or Vesicare respectively; the certified method of dissemination for the material incorrectly identified health professionals including via representatives, but the material was used as part of the patient support programmes managed by the agency. There was never a discussion with, or direction provided to, the agency that the material would be distributed in any other way.

Astellas understood that the agency's intention in publishing the material on its website was to market its abilities and was driven by a new creative director who was not trained on the Code. Astellas had not been aware of this previously; the agency had not asked the company if it could use its materials in this way. Astellas immediately asked the agency to remove the material which it did on the same day.

Astellas stated that the webpage went live on 15 April 2016 and was taken down on 22 September 2016; during the 27 weeks that it was available with unrestricted access, 116 visits were recorded. The agency did not solely work within the pharmaceutical industry and therefore it was likely that individuals from other industries, who Astellas UK considered members of the public, had accessed the site during that time.

Astellas's investigation also revealed that the agency had used imagery from another Astellas programme which was closed on 22 May 2016 (Remind Me). This imagery was displayed from 15 April 2016 until 22 September 2016 and was visited 121 times. This identified Astellas medicines within the transplantation area and included product brand names and a claim.

Although the PMCPA recognised in Cases AUTH/2576/2/13 and AUTH/2679/11/13 that agencies might wish to highlight their work, Astellas considered that the use of the brand names and therapeutic indications on the agency website went beyond any requirement to market creative capabilities and constituted promotion of prescription only medicines to the public, in breach of Clause 26.1. In addition, given the seriousness of this, Astellas UK could understand that the Panel might wish to consider the requirements of Clauses 9.1 and 2.

The agency confirmed that it had not discussed this with, or sought prior permission from, Astellas for the use of the graphics or their presentation on its website. The agency staff were last trained on the Code in April 2016.

Whilst this material was published on the agency's website without Astellas UK's knowledge or approval, the company stated that it was fully accountable for the actions of its agencies and acknowledged the failing in this regard. Astellas stated that it would now review the working practices of all of its UK agencies in relation to compliance, and its oversight, to ensure that it maintained the high standards expected.

**RESPONSE**

Astellas explained that the material on the agency website featured on a page entitled 'Our Work' which was accessible from the home page. The home page itself did not signpost to this section or refer to the type of work featured in this section or to Astellas. 'Our Work' could only be accessed via the menu at the top of the home page. In the website section 'Our Work' there was no separation of the Astellas material from non-pharmaceutical work and no information was provided to highlight that the Astellas work was aimed specifically at the pharmaceutical industry.

The agency was trained on the Code in April 2016 by another pharmaceutical company prior to the introduction of its patient support programme. The training specifically focused on:

- Clause 2 in terms of the non-promotional nature of nurse support
- Clause 4 in relation to governing the limits of information given to patients
- Clause 16 on pharmacovigilance and the requirements of the marketing authorization holder to ensure all agencies acting on its behalf followed the guidelines on adverse event reporting and the timelines for doing so and
- Clause 19 relating to patient confidentiality.

Attendees were provided with a copy of the 2016 Code.

**PANEL RULING**

The Panel noted that an Astellas employee had found patient support materials for Betmiga and Vesicare on the agency's website after searching for the URL

for the Betmiga patient support programme (Fresh Start). In that regard the employee had actively searched the internet for specific material. Having discovered the Betmiga material and the Vesicare material on the agency website, Astellas then found material from the Remind Me programme which supported patients taking Prograf (tacrolimus) or Advagraf (tacrolimus SR) for the prophylaxis of transplant rejection. None of the material had been posted on the agency's website with Astellas's knowledge or permission.

The Panel noted Astellas's submission that the material on the agency website was in the 'Our Work' section, accessible only via the menu at the top of the home page. According to Astellas, the 'Our Work' section did not separate Astellas material from non-pharmaceutical work.

The Panel acknowledged that creative agencies were entitled to promote their work and that as a result, examples of pharmaceutical material might appear on their open access websites. Whether this was acceptable would depend on the circumstances of each case. The Panel considered it would be prudent if the potential for such use was addressed in the contract between the pharmaceutical company and its agency at the outset. The website in this case was the agency's own website and anyone could access it. Anyone who landed on the home page of the website would have to consciously look further for examples of the agency's work, including that of Astellas, by using the menu.

The Panel noted that the material shown on the website for Betmiga and Vesicare consisted of the front page of two patient support booklets aimed at those taking one or the other medicines. From the text below, which detailed the client, the brief and the solution, it was clear that both medicines were for the treatment of overactive bladder. The material shown for the Remind Me programme was the nurse guide. In the accompanying text, the brief was stated to be 'Increase drug adherence by finding a way to help transplant patients remember to take their Prograf or Advagraf medication ensuring their new transplant does not fail'.

On balance, despite medicines and their indication appearing on an open access website, the Panel did not consider that medicines had been promoted to the public; the website was not aimed at the public *per se*. No breach of Clause 26.1 was ruled. The company had not failed to maintain high standards. No breach of Clause 9.1 was ruled.

The Panel noted its rulings above and ruled no breach of Clause 2.

During its consideration of this matter, the Panel noted its concern about the claim that Prograf and Advagraf would *ensure* (emphasis added) that new transplants did not fail and questioned whether such an all-embracing claim for efficacy was acceptable in an agency brief. The Panel requested that Astellas be advised of its concerns in this regard.

**2 Patient support programmes**

**VOLUNTARY ADMISSION**

Astellas noted that until the events described in Point 1 above, it had run two patient support programmes; VIP, for all patients prescribed Vesicare and Fresh Start, for those prescribed Betmiga. The agency was engaged to develop material for both programmes and also to run them via its team of nurses who manned a patient support line. Both patient support programmes had now been terminated due to Astellas's concern in relation to its lack of oversight and support as detailed below. These issues became apparent during the investigation described above.

Issues about adverse event reporting at the agency was the subject of a separate investigation that was raised in March 2016 but there was no conclusive evidence to uphold the issues raised.

**Description of patient support programmes**

The patient support programmes were designed to support patients taking Vesicare (VIP) or Betmiga (Fresh Start). When the first prescription was filled, patients were given details on how to enrol in the relevant programme via a leaflet from their health professional or, in the case of the VIP, via the Vesicare patient information leaflet and carton. Patients could enrol either by telephoning a careline manned by the agency staff or by going to a website, hosted by the agency, and certified by Astellas; in both cases, patients could only register on the programmes if they provided a batch code from their medicine packaging. This ensured that the programmes were only available to those already prescribed the relevant medicine.

Once registered, patients would receive a welcome pack and a call from a nurse at weeks 3, 7 and 11 to discuss their treatment and any questions they might have. After three months, proactive contact by a nurse as part of the patient support programme stopped, however patients were able to call the nurse support line at any point during their treatment (either during that three month period or beyond).

**Astellas oversight of patient support programmes**

A master services agreement (MSA) was put in place between Astellas and the agency in 2010, initially to cover the Vesicare patient support programme (VIP); although the programme had operated since 2006, no record of a contract with the agency before 2010 could be found.

When the programme started in 2006 the nurses on the patient support line were trained on the Vesicare summary of product characteristics (SPC) as well as on adverse event reporting. This was face-to-face training conducted by the Astellas medical and marketing department; training materials were also provided. In addition, nurses were given a 'script' to aid their discussions with patients. Although the adverse event training was repeated once a year via an Astellas pharmacovigilance training slide deck, which was rolled out to all the agency

nurses and confirmed back to Astellas that this had been completed, there was no record of any further training on Vesicare despite the SPC having changed nine times. Although Astellas had not provided revised SPCs to the agency over this period, the agency had confirmed that if nurses were asked a question about Vesicare which needed reference to the SPC then this would always be viewed online via the electronic medicines compendium (eMC) website to provide the latest information.

In 2013, the Fresh Start patient support programme was introduced for patients prescribed Betmiga. This coincided with the launch of Betmiga and, as with all new chemical entities, material was pre-vetted by the Medicines and Healthcare products Regulatory Agency (MHRA), including material for the patient support programme.

The nurse support line for Fresh Start was also staffed by the same agency nurses as the VIP programme, although Astellas had no copy of an MSA that reflected this additional arrangement. However, the additional arrangements were covered via estimates provided relating to the project and the approval of the relevant purchase orders (including Astellas standard Terms and Conditions). Astellas understood that in 2013 the nurses on the patient support line were trained on the Betmiga SPC current at that time. This face-to-face training was conducted by the medical and marketing department and training material was provided. As with the Vesicare training, there was no record of any further training on Betmiga, despite the SPC having changed six times. Although Astellas had not provided revised SPCs to the agency over this period, the agency had confirmed that if nurses were asked a question about the medicine that needed reference to the SPC then it would always be viewed online via the eMC website. In addition, nurses were provided with a 'script' to aid their discussions with patients; however, as identified below, this had not been kept up-to-date.

Although Astellas had monitored the number of patients enrolled into each patient support programme monthly and had continued to pay the agency the monthly fixed fee, it had not provided similar ongoing oversight and support for the nurse helpline in relation to product training. Whilst Astellas recognised that these programmes should have had ongoing consistent oversight, they had been managed by a series of colleagues without appropriate handover or training which had led to the current situation.

Astellas considered that, given that the nurses interacted directly with patients, this was a failure to maintain high standards, contrary to the requirements of Clause 9.1. Astellas also understood that the Panel might wish to consider the requirements of Clause 2 in relation to this lack of oversight and supervision.

**Patient support programme materials**

The material relating to VIP and Fresh Start was provided. Given that all material was printed/produced and sent out by the agency, Astellas did not keep any copies of the material at its offices. Astellas would receive an invoice as and when there was a need to print more material. The last such invoice was received in March 2014 for materials for the VIP programme and December 2015 for the Fresh Start programme.

**VIP**

Astellas had reviewed all of the VIP patient support programme materials and found that four job bags were, in error, set up as items that would be used only once, rather than those that would require re-approval if still in use before the end of the two year period post-certification (Clause 14.5). Details were provided.

Material set up in such a way was automatically withdrawn on Zinc after a stated time period, without those who might have it in their possession being notified. In addition, such material would not be flagged in Zinc as requiring re-approval, meaning in this case that some materials that were, until recently, still being used by the agency and sent to patients on the VIP patient support programme, had in fact been withdrawn on Zinc and had gone past the two year period before which they would need to be re-certified.

Astellas reviewed all VIP material including that withdrawn in March 2014 and considered that the content of these items was still appropriate for use; however, the above job bags were of a very poor quality regarding the way they had been set up including incorrect audience, poor information on objectives and having been initiated as a promotional item, contrary to Clause 9.1, and the material was in continued use past the two year period noted above, contrary to the requirements of Clause 14.5.

Astellas had also identified a number of other issues relating to four other materials for the VIP programme. Details were provided.

Astellas submitted that human error might have contributed to why certain job bags were set up or withdrawn inaccurately in Zinc and, in view of this finding, the company would continue to emphasise to staff the importance of appropriate job bag creation in relevant training. In addition, Astellas had incorporated these specific requirements into its peer review checklist to ensure that the quarterly reviews of job bags that were conducted internally assessed accurate job bag set up including the 'one-off use' status in Zinc.

**Fresh Start**

Astellas had reviewed material relating to the Fresh Start patient support programme and was concerned that the frequently asked questions section of the nurses' script (certified on 21 July 2015) no longer accurately reflected all adverse events listed in the current SPC (nausea was omitted). In addition, the Betmiga SPC was updated in April 2016 and the nurses' script was not revised to reflect the addition of a number of common side effects (constipation,

diarrhoea, headache and dizziness). Both of these omissions were attributable to human error by the signatory in the first instance and the owner of the material in the second; the issue was being addressed with both.

Astellas thus considered that the nurses' script was inaccurate and did not reflect the available evidence in relation to side effects, contrary to the requirements of Clauses 7.2 and 7.9. In addition, this amounted to a failure to maintain high standards, in breach of Clause 9.1 and had the potential to impact on patient safety, which would be contrary to the requirements of Clause 2. Impact on patient safety would be a matter of a separate assessment and communication with the relevant competent authorities where required.

Astellas also discovered that one item from the Fresh Start programme was, in error, set up as an item that would be used only once, rather than one that would require re-approval if still in use before the end of the two-year period post-certification. This item had therefore been used past the two year period.

In addition, two items were identified in April 2016 that still described Betmiga as 'new' at re-certification having been previously been re-certified in April 2014. These materials were immediately withdrawn. Astellas recognised that the word 'new' should have been removed from this material by February 2014 and thus after this date the material was in effect in breach of Clause 7.11. In addition, one item which was for re-certification was withdrawn to be updated with the new side effects and two other items had been withdrawn in error but remained active.

Astellas considered that, given that these materials were distributed to patients, as well as being contrary to the requirements of Clause 7.11, this amounted to a failure to maintain high standards, contrary to the requirements of Clause 9.1. Astellas also understood that the Panel might wish to consider the requirements of Clause 2 in relation to this lack of oversight and supervision.
In addition, Astellas found out on 26 August 2016 that the agency had been sending a survey to patients after 3 months on either programme. This had happened since the programmes were initiated and was intended to collect patient feedback on each programme. This information was previously provided to Astellas and outcomes from the questionnaire used in a promotional piece of material in 2009. As soon as the current team became aware, it instructed the agency to discontinue this activity immediately.

**RESPONSE**

Regarding Clauses 14.1 and 14.3, Astellas confirmed that all of the materials at issue were electronically certified before use. Not all materials were certified in a hard copy final form before use in breach of Clauses 14.1 and 14.3. Copies of all electronic certificates and hard copy certificates, where available, were provided for the items referred to above. As detailed in the sections below, some materials were withdrawn in Zinc in error but remained in use post the Zinc withdrawal.
Items related to the VIP and Fresh Start programmes and details of approval certificates

Details of the items were provided including whether the job bag was available at Astellas and whether a 'Hard copy (signed) certificate available' which denoted that a signed copy of the Zinc final certificate was contained within the job bag. These certificates were signed by a brand manager and not by a nominated signatory.

Astellas explained that the withdrawal dates for the items mentioned above referred to the date withdrawn from Zinc. Items were withdrawn from use at various times between the Zinc withdrawal date and the withdrawal of the whole programme. Details were provided of the eight VIP materials and the six Fresh Start materials where the withdrawal dates in Zinc did not match the withdrawal from use dates.

The Fresh Start website content was withdrawn from use on 1 April 2016 and subsequently withdrawn from Zinc on 4 April 2016, whilst an update was made to remove the word 'new' and reflect the most recent SPC. It was replaced by the holding page which was certified and went live on 11 April 2016 and remained in place until the closure of the programme. There was no site available between 1 and 11 April.

No patient support packs or letters were sent to patients after 22 September 2016 and no new patients were registered on either programme after the closure date on 10 October 2016.

**PANEL RULING**

The Panel noted that Astellas's oversight of the agency nurses who delivered the two patient support programmes was extremely poor. Although when both programmes first started, the nurses who were to man the helplines were trained on the relevant medicine (Betmiga or Vesicare), they received no further product specific training despite the fact that the SPCs for both products had since changed a number of times; some of those changes related to changes to Section 4.8, Undesirable effects. Further the telephone scripts which they had initially been given had not been revised; the script for the VIP helpline was dated October 2012. The script for the Fresh Start programme was dated March 2013 and did not reflect the addition to the Betmiga SPC of a number of common side effects (constipation, diarrhoea, headache and dizziness). Both scripts were thus inaccurate and out-of-date and in that regard the Panel ruled a breach of Clause 7.2. The Fresh Start script did not accurately reflect up-to-date information on possible side effects and in that regard the Panel ruled a breach of Clause 7.9. The Panel noted Astellas's submission that if nurses were asked questions about Betmiga or Vesicare that needed reference to the SPC, they would access the eMC website for the latest version. The nurses did receive annual training on adverse event reporting, certainly in relation to VIP. It was unclear whether

this had been updated annually, a copy had not been provided. It was also unclear why training on other matters outlined above had not been provided. Overall the Panel considered that such inadequate training of those who were expected to interact directly with patients was wholly unacceptable. High standards had not been maintained. A breach of Clause 9.1 was ruled. The Panel further considered that the failure to properly train the nurses and keep them updated with product changes was such as to bring discredit upon and reduce confidence in the pharmaceutical industry. It was crucial that out of all of the options available, patients could rely completely upon the industry for up-to-date and accurate information about their medicines. A breach of Clause 2 was ruled.

In addition to its failure to properly train the nurses who manned the helplines, the Panel noted that Astellas's oversight of the patient support materials was very poor. In that regard the Panel noted Astellas's submission that materials had been set up wrongly in Zinc such that although they were withdrawn in Zinc, mostly in 2014, they continued to be used by the agency beyond two years without being re-certified. In that regard the Panel ruled a breach of Clause 14.5.

The Panel further noted that some of the Betmiga material which was in use up to April 2016, continued to describe the medicine as 'new' when in fact that description could only be used for one year and should have been removed from the material in February 2014. A breach of Clause 7.11 was ruled. The Panel noted its rulings with regard to the oversight of material. The Panel noted that despite the withdrawal of certain materials in Zinc, the company had nonetheless paid the agency for the cost of printing materials for the Fresh Start programme in 2015. The Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The supplementary information to Clause 14.1 stated that when certifying material where the final form was to be printed companies could certify the final electronic version of the item to which no subsequent amendments would be made. When such material was printed the company must ensure that the printed material could not be used until any one of the company's signatories had checked and signed the item in its final form. In such circumstances the material would have two certificates and both must be preserved. The Panel noted Astellas's submission that not all materials were certified in a hard copy final form before use and those that were, were signed by the relevant brand manager and not by a nominated signatory. Further, the Panel noted that the patient satisfaction surveys had not been certified at all as no job bag had been raised in Zinc. The Panel ruled a breach of Clause 14.3. High standards had not been maintained. A breach of Clause 9.1 was ruled. As the material at issue was not promotional material, Clause 14.1 was not relevant and so the Panel ruled no breach of that clause.

The Panel noted its rulings and comments above. In the Panel's view, a certification process, correctly implemented, underpinned self-regulation. The Panel noted the number of materials which had not been correctly processed through Zinc, and some that had not been through Zinc at all. In that regard the Panel considered that Astellas's lack of control of material was such as to bring discredit upon, and reduce confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

**3 Transparency and disclosure**

**VOLUNTARY ADMISSION**

During its investigation into the issues noted above, Astellas found out that the nurses manning the support line for both patient support programmes still also worked for the NHS. This was not previously known, and Astellas considered that this additional information meant that the agency fitted the definition of an institution, organisation or association of health professionals noted in Clause 21. This clause required that any transfers of value made to such bodies in relation to services that they provided on behalf of a company were disclosed in accordance with the requirements of Clause 24. This disclosure had not taken place for transfers of value made to the agency in 2015, in breach of Clauses 21 and 24. Additionally, Astellas had found out that payments made to pharmacies in relation to enrolment of patients onto the Fresh Start programme had not been disclosed. The company stated it was addressing this and would upload the relevant data to the ABPI central platform as soon as possible.

**RESPONSE**

With regard to payment, Astellas explained that £7.50 was paid for each eligible patient enrolled on Fresh Start to pharmacies through the specific local pharmaceutical committees (LPCs) that Astellas worked with. To be eligible, patients must have been enrolled within 6 months of taking Betmiga. In 2015, 25 patients were enrolled, ie 25 payments were made. In 2016 only 1 patient was enrolled via a pharmacy. The same payment amount and eligibility criteria applied to the Vesicare programme. Only one LPC was involved in pharmacy enrolment for VIP during the period 2015 to 2016; it enrolled 5 patients via pharmacies in 2015 and 3 in 2016.

In response to a request for further information, Astellas explained that its agency had a UK business address and engaged the services of health professionals (nurses) to deliver support services to patients. In its capacity as an agency to deliver the patient support programme for Astellas the nature of its work was to deliver healthcare services to patients via a telephone support line. In Astellas's view the definition of a healthcare organisation as stated in Clause 1.9 applied.

Astellas noted that Clause 21 covered:

> 'Contracts between companies and institutions, organisations or associations of health professionals under which such institutions, organisations or associations provide any type

of services on behalf of companies *(or any other type of funding by the company not otherwise covered by the Code) are only allowed if such services (or other funding)'* [emphasis added].

Astellas acknowledged that Clause 21 referred to, *inter alia*, the requirements of Clause 19.1 (which covered medical and educational goods and services (MEGS)); however, it considered that it was also a 'catch all' clause to cover transfers of value (ToVs) made to a healthcare organisation that was not covered in any other clause of the Code. Given that Astellas did not know exactly how much was paid to each nurse, it considered that Clause 21 was relevant, even if the services provided were not related to MEGS.

Astellas submitted that the identity of individuals who were initially trained could be accessed by Astellas from the training records provided by the agency.

The agency offered nurse teams to its clients. The Astellas support lines were adapted to the needs of patients with overactive bladder, however the agency had confirmed that the provision of nurses via a support line was not a unique offering to Astellas and that the nurses were not sub-contracted from another agency/organisation. The agency engaged directly with the nurses manning the telephone support line.

Within clause 19.1 of the MSA the agency must gain prior consent from Astellas in order to sub-contract works. No such requests are known to have been made to Astellas.

Astellas submitted that it did not have the relevant information to be able to make a disclosable ToV to the nurses either in aggregate nor individually; Astellas only knew what it had paid to the agency.

The methodological note outlining how Astellas disclosed ToVs in these situations was publicly available on the ABPI website and stated:

'Where services for Astellas are rendered by an HCP [healthcare professional] on behalf of an HCO [healthcare organisation] (for example, Astellas enters into a service contract with an HCO and the services are provided by the HCO's employee), the associated fees and expenses paid by Astellas to the HCO are disclosed as Transfers of Value made to the HCO. This is the case unless Astellas can confirm that the HCP received a benefit from the Transfer of Value, either directly from Astellas or via the HCO, (e.g., fees paid to the HCP in connection with the services he/she rendered and/or reimbursement of any related expenses the HCP incurred), in which case Astellas discloses those Transfers of Value as being transfers to the HCP. Where Astellas can identify the HCP and know that the HCO will make the full Transfer of Value to the HCP on Astellas' behalf, the Transfer of Value is disclosed as being a Transfer of Value to the HCP.'

**PANEL RULING**

The Panel noted that the nurses who manned the patient helplines had been supplied by the agency. Astellas did not know how much of the fee it had paid the agency had gone either to the nurses as a group or to each individual nurse. At the start of the patient support programmes, Astellas had known who the nurses were through face-to-face training for the VIP programme (2006) and the Fresh Start programme (2013).

The Panel noted that the Code required companies to declare transfers of value made directly or indirectly to health professionals and healthcare organisations located in Europe. The definition of healthcare organization as stated in Clause 1.9 included 'an organization through which one or more health professional or other relevant decision makers provide services'. In that regard, the Panel considered that although creative agencies would not normally be considered healthcare organisations, in this case the nurses on the patient helplines had provided their services through the agency. In that regard the Panel considered that Astellas must declare the amount paid to the agency for the nurses on the ABPI central platform in accordance with Clause 24.1. If the company became aware of the individual identity of the nurses then the amount paid should be declared for each individual. It was unacceptable that the contract with the agency did not appear to be such that the company could identify the amount(s) paid. The Panel further noted that monies paid to pharmacies in relation to the enrolment of patients into the Fresh Start programme had not been declared. A breach of Clauses 21 and of 24.1 was ruled.

* * * *

The Panel was extremely concerned about is rulings and comments above. Some of the matters raised went to the heart of self-regulation and patient safety. The company's oversight of the patient support programmes at issue had been lamentable. Notwithstanding the fact that Astellas UK was currently suspended from membership of the ABPI and already undergoing a series of audits of its procedures under the Code, the Panel decided, in accordance with Paragraph 8.2 of the Constitution and Procedure, to report the company to the Appeal Board for it to consider whether further sanctions were appropriate in this case.

**COMMENTS FROM ASTELLAS UK ON THE REPORT FROM THE PANEL**

Astellas fully accepted and agreed with all of the Panel's rulings and sincerely apologised for the issues highlighted in this case. Astellas noted the Panel's comment that its oversight of the patient support programmes was lamentable. Whilst the patient support programmes were established some years ago, Astellas recognised that this was no excuse for the findings in this case.

Astellas had been aware for some time of failings in its review and certification process, both in relation to the quality of material and the technical accuracy of setting up a job bag in Zinc. In that regard it had, since 6 June 2016 regularly monitored the situation and shared findings with all relevant staff with the aim of achieving continuous quality improvement.

Astellas recognised the lack of oversight in relation to the patient support programmes at issue and acknowledged that this was due to its failure to provide clear process and training on the development, implementation and oversight of such programmes. When it discovered the issues in this case, Astellas ceased all patient support programmes and no more would be developed and put in place until such training and process had been implemented.

In relation to the transfers of value that had not been disclosed, Astellas submitted that all of those made to the agency as a healthcare organisation would be uploaded to the Astellas 2015 disclosure report on the ABPI portal, including the payments made to the nurse teams and pharmacies in running the programme.

At the consideration of the report the representatives from Astellas UK apologised to the Appeal Board for the failures outlined above which it accepted could bring discredit upon or reduce confidence in the industry.

Astellas stated that it was lamentable that due to process failure and human error its oversight of the patient support programmes fell well below acceptable standards and some of the matters raised went to the heart of self-regulation and patient safety.

Astellas knew that from previous PMCPA audits, there had, historically been issues with the company culture and processes relating to compliance. Astellas recognised that projects initiated some years ago did not have the rigour of oversight that it would apply to projects initiated today.

Astellas noted that this issue had come to light because an agency that it had worked with for many years had posted materials, which included brand names and indications, on its website without the company's knowledge or approval. However, once Astellas became aware of this issue it carried out a full investigation and self-reported all the related potential breaches of the Code.

Astellas did not seek to defend its actions taken in 2006 and 2013, or since, nor did it provide excuses. Astellas gave reassurance that it had learned from these events and although the journey to improve its compliance with the Code by addressing its culture and processes was in no way complete, progress had been made. Astellas submitted that the progress had been acknowledged by the Appeal Board and the ABPI Board. Events such as this made Astellas even more determined to get it right.

Astellas stated that the current UK team took full responsibility for these events and it sincerely apologised for these failures.

The representatives from Astellas UK stated that to help ensure that such failings did not recur, the company either planned to start or had a number of new processes and procedures in place including annual examinations for signatories, compliance risk assessments, compliance monitoring and regular material quality review. In addition, all job descriptions would be amended to include specific compliance training for the role and reporting structures for key roles including, *inter alia*, those for ethics and compliance, would change such that staff would report directly to global.

**APPEAL BOARD CONSIDERATION OF THE REPORT FROM THE PANEL**

The Appeal Board noted that this case had arisen from a voluntary admission by Astellas UK and the company had accepted all breaches of the Code including Clause 2. The Appeal Board also noted that Astellas UK had made a sincere apology for its failings in this case. However, the Appeal Board noted the Panel's comments and rulings above.

The Appeal Board considered that this case raised serious concerns about multiple failings and a complete lack of control in Astellas UK's review and certification process which was entirely unacceptable. In that regard the Appeal Board noted with concern a number of examples where signatories had taken an extremely short period of time to certify material in Zinc.

The Appeal Board was very concerned to note that Astellas UK had little or no knowledge about the qualifications of the nurses employed by its agency or of what they did or said to patients. Astellas should have had far greater oversight including feedback and audit of the nurses' interactions with patients. It was an appalling failure in particular that the nurses were not trained or updated on changes to the relevant SPCs. It was essential that patients could rely completely upon the industry for up-to-date and accurate information about medicines. The Appeal Board considered that the deplorable failure of process and oversight in this case raised serious concerns with regard to patient safety and public confidence in the pharmaceutical industry.

The Appeal Board noted that as a consequence of Case AUTH/2780/7/15 Astellas UK was currently suspended from membership of the ABPI. Astellas UK and Astellas Pharma Europe had each been audited twice (December 2015 and September 2016) and each would be audited again in April 2017. The Appeal Board was minded to report Astellas UK to the ABPI Board but given the exceptional circumstances, including that the re-audits in Case AUTH/2780/7/15 were due to be carried out very shortly, it decided that the issues that had arisen in this case should be looked at as part of the upcoming re-audit of Astellas UK, including examination of patient support programmes and certification of material. On consideration of the report of the re-audits the Appeal Board would reserve its decision on whether to report Astellas UK to the ABPI Board.

The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, Astellas UK should be publicly reprimanded for a lamentable lack of concern for patient safety and wholly unsatisfactory oversight and control of the patient support programmes and of the nurses employed to deliver them.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in April 2017 and the report was considered by the Appeal Board in May 2017.

The Appeal Board noted that Astellas UK and Astellas Europe were now working more closely and there was more open communication with staff. Both companies had been working to implement the recommendations of the previous audits and to ensure compliance was embedded. However, the Appeal Board noted the number of issues highlighted in the report and that there was still much work to be done.

The Appeal Board accepted that it took a long time to change culture but it was not convinced that progress was being made at an appropriate speed particularly given the issues that had come to light in Cases AUTH/2883/10/16, AUTH/2939/2/17 and AUTH/2940/2/17. This was particularly worrying given the level of scrutiny the companies were under. In the view of the Appeal Board, Astellas had much work still to do.

In relation to Case AUTH/2883/10/16 the Appeal Board decided that Astellas UK should be re-audited in October 2017 at the same time as the re-audit required in Case AUTH/2780/7/15 and the audit required in Cases AUTH/2939/2/17 and AUTH/2940/2/17 in relation to both Astellas UK and Astellas Europe.

In relation to Case AUTH/2883/10/16 the Appeal Board noted that it had reserved its position in relation to additional sanctions in this case until it had seen the report of the April 2017 re-audits. Bearing in mind that the case related to patient safety and a lack of control and oversight, the Appeal Board decided that in accordance with Paragraph 12.1 of the Constitution and Procedure, Astellas UK should be reported to the ABPI Board.

The Appeal Board noted the outcome of the audit in Case AUTH/2883/10/16, and the re-audits in Case AUTH/2780/7/15, the decisions to report Astellas UK to the ABPI Board in Cases AUTH/2883/10/16, AUTH/2939/2/17 and AUTH/2940/2/17 in relation to both Astellas UK and Astellas Europe. It also noted its concerns regarding the lamentable lack of concern for patient safety and wholly inadequate oversight and control. Whilst noting this was a matter for the ABPI Board, the Appeal Board's view was that Astellas UK was not ready to resume membership of the ABPI and the suspension should continue.

**ABPI BOARD CONSIDERATION OF THE REPORT FROM THE APPEAL BOARD**

The ABPI Board noted the rulings of breaches of the Code, the decisions of the Appeal Board regarding audit, re-audit and the public reprimand.

The ABPI Board agreed with the Appeal Board's comments and concerns about the re-audits in April 2017.

The ABPI Board noted and endorsed the Appeal Board's views about the total failure of the companies' systems in relation to the control of prescribing information, the lamentable lack of concern for patient safety, wholly inadequate oversight and control and initial lack of urgency. It was a woeful state of affairs.

The ABPI Board gave serious consideration to expelling Astellas UK from membership of the ABPI. However, it noted the commitments from Astellas Europe, the global company and of the new UK General Manager. The companies had made voluntary admissions and it was now imperative that the October re-audits showed significant progress.

The ABPI Board decided that it would extend the suspension of Astellas UK from membership of the ABPI for another 12 months. This further period would run uninterruptedly from the initial period of suspension and would then amount to the maximum suspension (two years) allowed under the ABPI Articles of Association.

The ABPI Board also decided that it wanted sight of the report of the October 2017 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of 2017. If the report of the re-audits did not show significant improvement and progress at both companies, then the ABPI Board would consider expelling Astellas UK from membership of the ABPI. The companies should consider undergoing an external assessment of progress, particularly in relation to risk management of compliance in the broadest sense, ie including matters beyond the scope of the Code, with the outcome to be available at the time of the October 2017 re-audits.

The ABPI Board also decided that the MHRA should be advised of the ABPI Board's very serious concerns about the conduct of Astellas UK and Astellas Europe particularly in relation to the matters concerning patient safety. EFPIA should also be updated and asked to ensure the EFPIA Board was informed of the position.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in October 2017 and the report of the re-audit was considered in November. The Appeal Board noted that as these were the fourth audits of the companies and given that Astellas UK was currently suspended from membership of the ABPI, it expected substantial progress and improvements from both companies. This expectation had not been met. The Appeal Board acknowledged that some progress had been made. The companies must take prompt action to implement the findings and recommendations in the report of the October 2017 re-audits.

The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been positive changes in the company culture. However, it was not convinced that the expected progress was being made, especially since the April 2017 re-audits.

Overall, the Appeal Board's view was that the rate of progress was inadequate and that the companies were not where they should be. There was still much work to do. The Appeal Board queried whether there was an element of structural inertia or perhaps fear of wrongdoing which was inhibiting or slowing the rate of progress.

Despite its criticisms, the Appeal Board noted the positive steps taken by the leadership of Astellas to engage more broadly with staff and drive changes.

The Appeal Board decided that both companies should be re-audited in April 2018. At which point it expected the 2018 global staff survey to demonstrate improvements at Astellas Europe and Astellas UK.

Whilst noting that this was entirely a matter for the ABPI Board, the Appeal Board's view was that if the report of the October 2017 re-audits and Astellas' response had come at the end of the two year suspension limit, then Astellas would have fallen well short of the standard required to resume membership of the ABPI. Unless substantial progress was seen in the report of the re-audits in April 2018, in the Appeal Board's view, Astellas UK would be at serious risk of a recommendation that it be expelled from membership of the ABPI.

**ABPI BOARD FURTHER CONSIDERATION**

The ABPI Board noted the Appeal Board's comments and concerns about the re-audits in October 2017 and the additional information provided by Astellas.

With regard to the external assessment of progress, particularly in relation to risk management of compliance in the broadest sense ie including matters beyond the scope of the Code, the ABPI Board noted the information provided by Astellas.

Following a change in tone from the top of Astellas, the ABPI Board recognised that meaningful progress had been made by the companies. The ABPI Board understood the difficulty inherent in making wide-sweeping cultural changes, and how long it took for those changes to become fully embedded within a large organisation. However, the ABPI Board acknowledged Astellas' clear commitment to further improvement.

The ABPI Board noted Astellas' statement that its materials were compliant in May 2017 in relation to issues of patient safety.

The ABPI Board also decided that it wanted sight of the report of the April 2018 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of the current suspension in June 2018.

The ABPI Board decided that taking all the circumstances into account it would take no further action at this stage in relation to the expulsion of Astellas from membership of the ABPI. The suspension from membership of the ABPI would remain in place until June 2018.

The ABPI Board also decided that the MHRA should be advised of the position. EFPIA should also be updated and asked to ensure that the EFPIA Board was informed of the position.

**APPEAL BOARD FURTHER CONSIDERATION**

In response to a request from the Appeal Board Astellas provided further information which showed that matters raised by the Appeal Board in November were being addressed more promptly than previously indicated.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in April 2018 and the report of the re-audits was considered in May 2018.

The Appeal Board noted the detailed responses from Astellas to the report of the April 2018 re-audits including that it was an accurate reflection of the work undertaken.

The Appeal Board noted the results of the 2018 staff survey and the progress made. Numerical increases had been shown in a number of parameters since the previous survey in July 2017. There were concerns about the comments made by staff. The Appeal Board also noted the differences in the Astellas UK results which were generally better than the Astellas Europe results. The Appeal Board considered that the Astellas Europe management committee scores although improved were still not where they should be.

The Appeal Board noted the comments in the report of the April 2018 re-audits and considered that both the leadership of Astellas Europe and Astellas UK had engaged with staff to bring about progress. There was still work to be done. The Appeal Board noted one of the recommendations was that members of the leadership team at Astellas Europe should be held to account and be challenged on compliance matters.

The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been further positive changes in the company culture and this needed to be continued. The Appeal Board noted that there had been some positive compliance initiatives. The discussion fora and communications continued and progress had been made including ensuring staff had time to complete training.

The Appeal Board noted that whilst as a percentage there had been a significant increase in the number of job bags, the overall number was still low. As Astellas increased its activities it must remain extremely vigilant to compliance requirements in particular in relation to certain higher risk activities such as patient support programmes, product launches etc. The true test of the compliance framework in Astellas and its approach would be when activity levels including higher risk activities were increased and the company was operating at business as usual.

The Appeal Board considered that, at long last, the re-audits in April 2018 showed that progress had been made and that the companies were building on momentum started in summer 2017.

The Appeal Board was concerned that these were the fifth audits of each company and that the first audits were in December 2015. It was extraordinary that it had taken so long to demonstrate meaningful change. The overall impression from the report of the April 2018 re-audits was that Astellas was showing improvement and momentum. However, whilst the companies had reached a certain level, given all the circumstances including that Astellas UK had been suspended from membership of the ABPI and that the Appeal Board still had concerns, the Appeal Board decided that Astellas Europe and Astellas UK should each be re-audited at the end of the first quarter of 2019 to ensure that the improvements and the momentum continued and were built upon.

On the information before it, and noting that Astellas UK was still to respond to the PMCPA in relation to matters raised following completion of the consideration of a complaint concerning Astellas UK, Case AUTH/2984/10/17, the Appeal Board decided that sufficient progress had been made by the companies such that the Appeal Board did not consider that it warranted a recommendation for the expulsion of Astellas UK from membership of the ABPI when the matter came before the ABPI Board on 5 June 2018.

**ABPI BOARD FUTHER CONSIDERATION**

In June 2018 the ABPI Board noted the comments from both the Appeal Board and Astellas. The ABPI Board noted the limited information provided about matters raised in Case AUTH/2984/10/17. This was still to be considered by the PMCPA and the Appeal Board and was not before the ABPI Board for consideration.

The view of the Appeal Board was clear. The ABPI Board agreed with the Appeal Board's views and assessment of the re-audits and concluded that meaningful progress had now been made.

The ABPI Board believed that the culture in the companies had improved and noted that much of this had been led by the General Manager of Astellas UK. However, the Board recognised the importance of an ongoing commitment to ensure sustained culture change. On reviewing all the material, the ABPI Board had concerns about the sustainability of the changes made given that there had already been five audits/re-audits, and especially as further types of activity were still to be fully re-introduced across the companies.

The ABPI Board therefore decided that it wanted to see the report of the 2019 re-audits and be informed of major developments including the outcome of Case AUTH/2984/10/17.

In the circumstances, there was no need for the ABPI Board to consider expelling Astellas UK from membership of the ABPI. The suspension would end on 24 June 2018 and Astellas would revert to full membership of the ABPI.

Astellas should be cognisant of this ongoing sustainability requirement and monitoring (particularly in light of the matters still to be concluded in Case AUTH/2984/10/17) when communicating about the Board's decision.

The ABPI Board also decided that the MHRA should be advised of the position and that EFPIA should be updated and asked to ensure that the EFPIA Board was informed of the position.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in April 2019 and the report of the re-audits was considered in May 2019.

The Appeal Board noted the detailed response from Astellas Europe and Astellas UK to the report of the April 2019 re-audits.

The Appeal Board noted two new senior appointments; a new President EMEA Operations who joined Astellas in July 2018 and a new General Manager, Astellas UK who was appointed from April 2019.

The Appeal Board noted from the report of the April 2019 re-audits that it appeared that a more compliant culture was embedded within Astellas with improved communication. It was essential that this was maintained.

The Appeal Board considered that Astellas UK must ensure a proper professional approach to investigating and responding to any complaint under the Code such that the shortcomings in Case AUTH/2984/10/17 were not repeated. The Appeal Board noted that an audit had not been required in Case AUTH/2984/10/17. The case had, in accordance with established practice, been discussed as part of an examination of the company's culture at the re-audits.

The Appeal Board noted that these were the sixth audits/re-audits of each company and that the first audits were in December 2015. The Appeal Board considered that, on the information provided in the report of the April 2019 re-audits, it appeared that the companies had made further improvements, that this would be maintained and broadly the companies were where they should be. The Appeal Board, however, remained very concerned about the amount of time it had taken Astellas to reach this point. The Appeal Board noted that Astellas stated that it would follow up on the issues identified in the report of the April 2019 re-audits and it was committed to maintaining its approach to embedding a sustainable compliance culture. The Appeal Board noted a number of activities/actions were due to be undertaken. On the understanding that this work was completed, that the progress shown to date was continued and a company-wide commitment to compliance was maintained, the Appeal Board decided that, on the basis of the information in the report of April 2019 re-audits, no further action

was required in relation to Case AUTH/2780/7/15, Case AUTH/2883/10/16, Cases AUTH/2939/2/17 and AUTH/2940/2/17.

The Appeal Board noted that the audit/re-audits in these four cases had been required by the Appeal Board. They had not been required by the ABPI Board. Nonetheless, the Appeal Board noted the ABPI Board's request to see the report of the April 2019 re-audits.

At the re-audits in April 2019 it was noted that the MHRA decided that Astellas advertising materials should be submitted for review. This was introduced for all new materials issued since 1 December 2018.

**ABPI BOARD UPDATE**

In June 2019 the ABPI Board received an update as requested. It noted the comments from both the Appeal Board and Astellas and the improvements made.

| | |
|---|---|
| **Voluntary admission received** | **20 October 2016** |
| **Undertaking received** | **15 February 2017** |
| **Appeal Board consideration** | **16 March 2017, 25 May, 16 November, 7 December, 17 May 2018, 22 May 2019** |
| **ABPI Board consideration** | **6 June 2017, 5 December, 5 June 2018** |
| **ABPI Board update** | **4 June 2019** |
| **Interim case report first published** | **3 May 2017** |
| **Case completed** | **22 May 2019** |

**CASE AUTH/2935/2/17**

# ANONYMOUS EX-EMPLOYEE v SUNOVION

## Promotion of Latuda

**An anonymous, ex-employee of Sunovion alleged that a regional business manager (RBM) encouraged staff to pressurise customers into prescribing Latuda (lurasidone) for schizophrenia by suggesting that if Latuda was not considered as part of a patient review, they might be sued by patients or patient groups. It was alleged that the RBM also encouraged staff to quote national guidelines which stated that a medication review should be considered if a patient had side-effects. The complainant was concerned that if such an approach was shared with customers, it could bring the industry into disrepute. The complainant added that the RBM cited a medico-legal presentation by a barrister as the basis and implied authority to challenge customers' prescribing.**

**The detailed response from Sunovion is given below.**

**The Panel noted that interview transcripts from those who had attended a recent regional meeting clearly showed that the majority recalled that the RBM had verbally directed the sales team to suggest that there might be legal consequences if patients were not reviewed and alternative treatment options offered. This was contrary to Sunovion's original submission that the interviews provided a mixed and unclear impression of what the RBM had stated.**

**The Panel noted that certain interviewees stated that the RBM referred to the barrister and instructed the team to engage him/her in customer meetings to make customers feel uncomfortable about their medico-legal position with regard to monitoring antipsychotics. The interview transcripts also stated that the RBM said that 'if they do not offer a change of treatment and make a note of it, it could come back and bite them' and 'the barrister's presentation was mentioned by the RBM as a way of endorsing this point'.**

**The Panel considered that on the balance of probabilities the RBM had not maintained a high standard of ethical conduct and his/her verbal direction advocated a course of action which would be likely to lead to a breach of the Code. Breaches of the Code were ruled.**

**As there was no information about what Sunovion staff had said to health professionals, the Panel considered that the complainant had not shown, on the balance of probabilities, that the representatives had not maintained a high standard of ethical conduct when promoting Latuda, despite the RBM's briefing. No breach of the Code was ruled in that regard.**

**The Panel further noted the allegation that the RBM had encouraged his/her staff to quote national guidelines that stated that a review of medication should be considered if a patient had side-effects. In the Panel's view, it was not necessarily unacceptable for companies to refer to the guidelines provided the manner in which it was done complied with the Code. The Panel noted that one interviewee stated that the RBM asked the team to use the guidelines as a tool to inform customers that they should consider switching treatment in patients with cardiovascular risk factors. It was not necessarily unacceptable under the Code for a company to promote a simple switch from one product to another. The Panel considered that the complainant had not shown, on the balance of probabilities, that in referring to the guidelines the RBM had advocated a course of action which would be likely to lead to a breach of the Code. No breach of the Code was ruled in that regard including no breach of Clause 2.**

**The Panel noted Sunovion's submission that referencing medico-legal consequences was not an acceptable approach to promote Latuda either directly or indirectly. The Panel noted its rulings above including that the complainant had not proved his/her complaint on the balance of probabilities in relation to the promotion to health professionals etc. In addition the Panel considered that its ruling of a breach of the Code in relation to the RBM covered the position regarding high standards. The Panel ruled no breach of the Code. The company had not brought discredit upon or reduced confidence in the industry and therefore the Panel ruled no breach of Clause 2.**

**Sunovion provided the requisite undertaking and assurance and the Appeal Board received the case report as set out in Paragraph 13.4 of the Constitution and Procedure.**

**The Appeal Board was very concerned to note that in its initial response to the Panel Sunovion did not provide an accurate summary of the interviews about the February sales meeting. This was only discovered when the Panel requested copies of the interviews conducted. The Appeal Board noted that self-regulation relied, *inter alia*, upon the provision of complete and accurate information but considered that the company's initial response was misleading. In that regard the Appeal Board's view was that additional sanctions under Paragraph 11.1 of the Constitution and Procedure should be contemplated. Sunovion should respond to these concerns in writing and it was invited to appear before the Appeal Board when the matter was considered. Sunovion was provided with a copy of the papers.**

**The detailed comments from Sunovion about the possible imposition of further sanctions is given below.**

**The Appeal Board noted the Panel's rulings of breaches of the Code. The Appeal Board noted that the company had apologised and admitted that it had made errors.**

**The Appeal Board noted that contrary to the written comments made by Sunovion in response to the concerns raised by the Appeal Board, the issue was that the summary was not a fair reflection of the interview transcripts, not that the transcripts had not been provided with the company's original response.**

**The Appeal Board asked the Sunovion representatives to explain how the interview transcripts from the six representatives could be summarised as giving a mixed and somewhat unclear impression of the verbal direction provided by the RBM when 5 of the 6 supported the complainant. This point had not been addressed by Sunovion.**

**The Appeal Board noted that in response to questioning the Sunovion representatives stated that the interviews were conducted by a senior UK director solely responsible for investigating this complaint. That director's findings were that although the picture was mixed and unclear there was a strong probability that the RBM had done something wrong and that, on the balance of probabilities, this was in breach of the Code. According to the company representatives, this was included in the initial draft of the company's response to the complaint which was sent to the US parent company. The US parent company decided, based on external legal advice that, in spite of self-regulation, it was not Sunovion's responsibility to prove the complaint. Although the US parent company did not see the interview transcripts it, nonetheless, altered the UK company's draft and denied breaches of the Code stating that the interviews provided a mixed and somewhat unclear impression of the verbal direction provided. Before signing the amended draft of the company's response, a senior European executive requested sight of the interview transcripts. Sunovion's representatives stated that when the senior UK investigating director had been shown the revised draft and advised of the legal opinion from the US he/she still stood by his/her original draft. The Appeal Board noted that the senior European executive stated that he/she was not an expert on the Code.**

**The Appeal Board considered that the responses of the company representatives to its questions were contrary to Sunovion's written submissions to the Panel and the Appeal Board and to the company's submission at the consideration of this matter that the summary of the interviews provided with the company's response to the complaint was a good faith attempt to set out the relevant facts. The company's presentation also stated that Sunovion supported the Code, was committed to compliance, self-regulation and transparency.**

**The Appeal Board noted that the senior UK investigating director's findings had been undermined by the US parent company which had not even seen the interview transcripts. At the Appeal Board hearing the US parent company representative acknowledged that it had compromised the professional integrity of the senior European executive. It did not stand behind the letter today. The US parent company representative also stated that many lessons had been learned and apologised. The Appeal Board was extremely concerned about the company's explanation. It considered that such a deliberately inaccurate, misleading and disingenuous response brought discredit upon and reduced confidence in the pharmaceutical industry. Whilst it might not be the respondent company's responsibility to prove a breach of the Code, it was the respondent company's responsibility to provide accurate information. Self-regulation relied, *inter alia*, upon the provision of complete and accurate information from pharmaceutical companies. The Appeal Board noted the submissions from the Sunovion representatives and it considered that the company's conduct in altering its response, contrary to that of the investigator and the clear evidence from the interviews, raised very serious concerns about system failure and company culture.**

**The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, Sunovion should be publicly reprimanded for providing inaccurate and misleading information to the Panel and Appeal Board. The Appeal Board also decided to require an audit of Sunovion's procedures in relation to the Code. The audit should include interviews with staff at the US and Japanese parent companies. The audit would take place in November 2017 and on receipt of the report the Appeal Board would consider whether further sanctions were necessary.**

**Sunovion was audited in November 2017 and on receipt of the audit report in January 2018 the Appeal Board questioned how seriously the whole Sunovion organisation was taking its commitment to self-regulation. The culture with regard to the Code and leadership on compliance matters needed to urgently improve across the organisation. The company in the US, Sunovion Pharmaceuticals Inc, and in particular the parent company in Japan, Sumitomo Dainippon Pharma Co, needed to demonstrate that the seriousness of the situation was understood and appropriate action taken.**

**The Appeal Board noted that the audit report highlighted many issues and concerns to be addressed including arrangements for advisory boards, certification, updating and compliance with standard operating procedures, role of medical science liaison staff, control and updating of material and attention to detail and management of all third-party service providers. Significant commitment was required to address these issues.**

**On receipt of further information in February and March 2018, and on noting the dates for completion of some of the actions etc, the Appeal Board decided that the company should be re-audited in June 2018.**

**On receipt of the report for the re-audit the Appeal Board would decide whether further sanctions were necessary.**

**Sunovion was re-audited in June 2018 and on receipt of the report of the re-audit in September 2018 the Appeal Board noted that Sunovion had made some meaningful progress and that there appeared to be a genuine wish to create a more sophisticated compliance infrastructure and to build on the improvements made. The Appeal Board noted that Sunovion had committed greater staff resource to help address its compliance needs. The Appeal Board welcomed the reported improved relationship between Sunovion and its US parent company.**

**The Appeal Board was again concerned about the inaccurate responses from the company with regard to its disclosure of payments to patient organisations at the re-audit and it noted the related issues that arose in Case AUTH/3027/3/18. It was paramount that Sunovion ensured its responses to the PMCPA were accurate.**

**The Appeal Board noted that the report of the re-audit still highlighted further important issues and concerns to be addressed including a review of its material, updating standard operating procedures, urgently address the company's apparent lack of understanding of the definition of promotion, review of the active materials list and further training. Significant ongoing commitment was required to address these issues.**

**The Appeal Board decided that Sunovion Pharmaceuticals Europe should be re-audited in April 2019. On receipt of the report of the re-audit the Appeal Board would decide whether further sanctions were necessary.**

**Sunovion was re-audited in April 2019 and on receipt of the report of the re-audit in July 2019 the Appeal Board noted that there had been significant progress at Sunovion since the re-audit in June 2018. The Appeal Board noted that Sunovion had a compliance action plan to address recommendations from the re-audit. The Appeal Board noted some actions were already completed and that others were due to be completed very shortly. On the basis that this work was completed, the progress shown to date was continued and a company-wide commitment to compliance was maintained, the Appeal Board decided that no further action was required.**

An anonymous, ex-employee of Sunovion Pharmaceuticals Europe Ltd alleged that one of the company's regional business managers (RBMs), encouraged his/her sales staff to exert undue pressure on customers to get them to prescribe Latuda (lurasidone). Latuda was an atypical antipsychotic indicated for the treatment of schizophrenia in adults aged 18 years and over.

**COMPLAINT**

The complainant alleged that the RBM in question encouraged sales staff to suggest to customers that if they did not consider Latuda as part of a patient review, prescribers could be open to being sued by patients or patient groups. The complainant considered that such behaviour was unethical; the sales team was being encouraged to use this approach to put pressure on the customer.

The complainant added that, in addition to the above, the RBM also encouraged his/her staff to quote Commissioning for Quality and Innovation (CQUIN) measures that stated that a review of medication should be considered if a patient had side-effects. The complainant queried whether this was part of a wider marketing strategy or supported by the senior staff. The complainant was concerned that if such an approach was shared with customers it could bring the industry into disrepute.

The complainant added that Sunovion used a named barrister to discuss medico-legal practice, as a presentation. The regional manager cited this in team meetings as the basis and implied authority to challenge customers' prescribing.

When writing to Sunovion, the Authority asked it to consider the requirements of Clauses 2, 9.1, 15.2 and 15.9 of the Code.

**RESPONSE**

Sunovion submitted that it was committed to compliance with the Code and took its obligations under the Code very seriously. Sunovion did not accept, endorse or encourage the manner of promotion described in the complaint. All employees received annual ABPI Code refresher training and training on the global code of conduct. The code of conduct encouraged open dialogue if an employee had any concerns, and also described a process for reporting concerns anonymously.

Sunovion stated that it placed a strong focus on providing effective training/clear briefings for its sales force. The company held three national cycle meetings per year led by head office and these were supplemented by local regional sales meetings led by RBMs but supported by head office as required.

In addition to product training/briefing on Latuda, Sunovion also endeavoured to train its staff to a high standard on the broader NHS policy requirements that health professionals might need to consider in daily practice so that staff were knowledgeable about the NHS and could better understand the challenges that health professionals might face.

Sunovion stated that following the investigation described below, it appeared that the main focus of the complaint was on a regional sales meeting that took place in February 2017. For thoroughness Sunovion had gone back to April 2016 to review briefing materials for all meetings, where there might have been content relating to promotion which involved the regional sales team in question. Sunovion explained that antipsychotics differed in their propensity to influence cardiovascular (CV) risk factors such as body weight, serum lipids and blood sugar. One of the national goals for the CQUINs scheme in 2016/2017 was improving the physical

health of patients with severe mental illness. This included identifying patients with schizophrenia who were at risk of CV disease and offering interventions. These interventions would include lifestyle modification and could also include considering a change in treatment to an antipsychotic with a lower metabolic-risk. Guidelines issued in 2016 by the British Association of Psychopharmacology (BAP) also endorsed this approach.

The promotional strategy for Latuda included discussion of the effects on blood lipids, blood glucose, and body weight and that the medicine might be an appropriate option for patients with CV risk factors.

Sunovion submitted that at the first national sales cycle meeting of the 2016/2017 business year (April 2016), the sales force was briefed on the strategy and campaign for the coming year led by head office. The presentations given during this meeting covered the metabolic consequences of antipsychotic treatment and focussed on the clinical and health economic benefits of low-metabolic risk antipsychotics. The presentations did not refer to medico-legal risk.

The second and third national sales cycle meetings took place in September 2016 and January 2017 respectively. The presentations given to the sales force did not refer to medico-legal risk. Refresher training on the Code was also provided by an external consultant.

With regard to regional sales meetings, three had taken place led by the RBM in question, June and December 2016 and February 2017.

The briefing/training presentation on In Call Quality was presented to the regional sales team in June 2016 and described a way of identifying patients for whom Latuda might be considered an appropriate treatment by referring to CQUINs. No reference was made to medico-legal risk. The briefing training presentation, 'Starting a Patient on Latuda' was presented at the same meeting and covered the high metabolic risk patient and described how to switch to Latuda from other antipsychotics. There was no reference to medico-legal risk. The sales meeting which took place in December 2016 was attended by the whole sales force ie both regional sales teams. There was no reference to medico-legal risk. Copies of all of the presentation was provided.

The presentations by the barrister were educational and intended to inform health professionals about the legal aspects of their work in treating patients with mental health problems. The barrister was an expert in the medico-legal aspects of managing mental health patients and had regularly spoken on this subject to NHS audiences in recent years, independent of Sunovion sponsored events. Sunovion provided one example of such an event.

In particular, one of the presentations covered the legal aspects of informed patient choice when prescribing. The barrister presented at Sunovion-sponsored meetings in October and November 2015 and March and September 2016.

The most recent regional sales meeting took place in February 2017. Sunovion interviewed three key account managers, a hospital sales representative and a market development manager, all of whom reported directly to the RBM and had been at the meeting. Sunovion also interviewed a medical science liaison (MSL) who reported to the medical department but also attended the regional sales meeting. The meeting agenda and a summary of the meeting written by the RBM was provided. Due to the workshop style of the meeting, and the nature of the agenda (ie a focus on team building and best practice sharing) there were no slides presented. In his/her interview the RBM gave a full and detailed account of his/her instruction and briefing to the sales team at this meeting. This involved identifying customer needs in a non-directive fashion, and the importance of understanding and acknowledging that different customers had different needs. One of the needs that might be identified was a requirement for a low metabolic-risk antipsychotic. The RBM stated that he/she did not direct the team to focus on this need, and did not direct the team to discuss the medico-legal implications of not intervening in patients at high risk. The RBM stated that he/she did not link high risk patients and treatment with Latuda with risk of legal consequences. He/she stated that he/she did not direct the team to use the barrister's presentation unless it was thought to be relevant to the educational needs of health professionals in their territories. This was consistent with the email summary of the meeting sent to the sales team after the meeting by the RBM.

Sunovion stated that the interviews with other members of the sales team provided a mixed and somewhat unclear impression of the verbal direction provided by the RBM at the meeting in February. While some thought that he/she had directed them to suggest that there might be legal consequences if patients were not reviewed and alternative treatment options offered, others did not.

Sunovion noted that it had found no evidence to suggest that the subject of the complaint had ever been used with health professionals.

In summary, Sunovion stated that:

- the sales force had received clear, periodic briefings/direction at a national level on the Latuda promotional campaign which were in line with the company's promotional strategy and with the Code. All presentations that related to promotion had been reviewed and certified.
- the sales force had received regular and periodic training on the Code, and their responsibilities (ie twice in the last 6 months).
- Sunovion had sponsored health professional meetings at which the barrister had spoken about medico-legal issues; he/she was a respected speaker in that area, the content of the presentations was in line with the Code and the presentations were certified.
- all presentations at all regional sales meetings in the current business year which related to Latuda promotion were in line with the company's promotional strategy and with the Code.

All presentations which related to promotion had been reviewed and certified.

- with regard to verbal discussion/direction from the RBM to the sales team, in particular at the regional sales meeting in February 2017, whilst there was no conclusive evidence either way, it was apparent that some of those at the meeting interpreted this verbal direction in a way not consistent with Sunovion's approved promotional campaign ie that referencing 'medico-legal consequences' was not an acceptable approach to promoting Latuda, either directly or indirectly. Sunovion also considered that the written email follow up summary of the meeting from the RBM to the sales team was not as clear as required to ensure total clarity in line with the approved company approach to promotion.

Sunovion submitted that there was no conclusive evidence that the alleged approach (ie a focus on 'medico-legal consequences' matters in the promotion of Latuda) had led to inappropriate conduct with health professionals. Sunovion noted that it was notified of this complaint on 15 February 2017 and it rapidly responded to investigate the complaint and in parallel it had re-briefed sales staff to reinforce the company's approved approach to promoting Latuda, specifically and that it was not acceptable to refer to 'medico-legal consequences' either directly or indirectly.

Sunovion denied breaches of Clauses 9.1, 15.2, 15.9 and 2. As detailed above Sunovion submitted that it had robust procedures in place, had investigated the matter thoroughly and had taken appropriate action to reinforce the high standards that it expected of all of its staff at all times.

In response to a request for further information, Sunovion reiterated that referring to 'medico-legal consequences' was not an acceptable approach to promoting Latuda, either directly or indirectly and this approach had never been communicated or endorsed by Sunovion or senior management. This approach had never been part of the strategy or brand plan for Latuda, and had never been part of any training or briefings delivered by the head office team. As noted above, verbal direction provided by the RBM to his/her team was interpreted by some individuals as asking them to follow the above approach, and the interviews reflect this.

Sunovion noted that the RBM at issue was no longer employed by Sunovion.

Sunovion addressed each point raised in the request for further information in turn:

**1 Details of the five meetings at which the barrister presented**

Sunovion provided details of the number of attendees at each meeting, the venue and the presentations delivered.

At one meeting, organised by the academic function of an NHS organisation, Sunovion only sponsored the barrister's session which was made clear on the agenda and was in line with the company's standard operating procedure (SOPs) for sponsoring meetings with health professionals. Sunovion was not involved in the other sessions/presentations at the meeting.

All of the other meetings were organised by members of the sales team from a logistics perspective which was in line with Sunovion's documented process and SOPs for sponsoring meetings with health professionals. The head office team was responsible for reviewing and certifying the speaker's presentation in advance of the meeting.

The meeting attendees were mainly psychiatrists, together with a small number of pharmacists and psychiatric nurses. The meeting objectives were as follows:

**October 2015, to provide education on:**

- the medico-legal issues faced by psychiatrists during their routine clinical practice.
- the clinical data on the use of Latuda in the treatment of schizophrenia in adult patients.

**November 2015, to understand:**

- the legal framework of the First Tier Mental Health Review Tribunal and hospital manager's hearings.
- the expectations of the different members of the panels when giving evidence.
- the importance of shared decision making in prescribing for mental health problems, including clinical data on the use of Latuda for the treatment of schizophrenia in adult patients and
- to allow attendees to be more confident when presenting evidence at mental health review tribunals and hospital manager's hearings.

**March 2016, to provide education:**

- the medico-legal issues faced by psychiatrists during their routine clinical practice.

**September 2016, (two meetings) to provide education on:**

- the medico-legal issues faced by psychiatrists during their routine clinical practice.
- the metabolic adverse effects of antipsychotics, including relevant data on Latuda for the treatment of schizophrenia in adult patients.

At the five meetings listed above, the barrister gave one of the two presentations Sunovion provided originally:

1 'Report writing and Presenting Evidence'.
2 'The Importance of Informed Patient Choice'.

Presentation 1 was delivered by the barrister at the meetings in October 2015, November 2015 and March 2016. Other presentations were delivered at these meetings either by an MSL or independent speaker. Sunovion noted that the presentation delivered by the MSL in October 2015, was a pre-

approved and certified slide deck used by the MSL team in the majority of its promotional presentations at the time. It was not tailored or specific to the event in question.

Presentation 2 was delivered by the barrister at the two meetings in September 2016 together with a presentation on the metabolic adverse effects of antipsychotics delivered by an MSL.

Copies of the meeting agendas, slides presented by Sunovion employees or Sunovion-sponsored speakers, and speaker contracts, were provided.

**2 Briefing of sales force on how to use the barrister's presentation**

Sunovion stated that it had a documented SOP and process for conducting sponsored meetings with health professionals in line with the Code, and members of the sales force had been trained, both as part of the induction process when they joined the company, and then approximately annually thereafter.

Sunovion submitted that it did not provide individual documented briefings to the sales force on how to hold a sponsored speaker meeting with each and every single potential individual speaker.

Sunovion trained/briefed the sales force on the SOP and process for conducting sponsored meetings with health professionals in line with the Code, and as part of this process, if there was a third-party speaker, (eg the barrister in this case), then that speaker's slides had to be reviewed and certified by head office in advance of the meeting to ensure that the context and content of the speaker's presentation was appropriate and code compliant.

There was no written briefing provided by the RBM regarding the use of the barrister's presentations. As noted above, Sunovion did not provide written briefings on how to use each and every individual speaker. Any 'briefing' was provided verbally as part of conversations with members of the team and was therefore not documented.

The barrister was used infrequently as a speaker for Sunovion. Sunovion did not provide written briefing or training on the use of his/her slides, but did review, approve and certify them in line with its SOP and processes.

Copies of speaker presentations were not routinely provided to the representatives or market development managers ie within the company's SOP, the MSL team and head office were responsible for liaising with speakers on slide presentations to review and certify in advance of the meeting.

Sunovion provided anonymised copies of the interviews conducted with members of the sales team, the MSL, market development manager, and RBM.

**PANEL RULING**

The Panel noted that the complainant was anonymous. The Constitution and Procedure stated that anonymous complaints would be accepted, but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties.

The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was often impossible in such circumstances to determine precisely what had happened.

In relation to the allegation that the RBM had encouraged sales staff to suggest to customers that if they did not consider Latuda as part of a patient review, prescribers could be open to being sued by patients or patient groups, the Panel noted the comments made by staff interviewed about the regional sales meeting in February. The Panel considered that it was disingenuous of Sunovion in its original response to state that the interviews with members of the sales team provided a mixed and somewhat unclear impression of the verbal direction provided by the RBM at the regional sales meeting in February. The Panel noted that anonymised copies of the interviews conducted with members of the sales team, the MSL, market development manager, and RBM were provided only in response to a request for further information and it was clear from these interviews that the majority of individuals at the meeting recalled that the RBM's verbal direction was that the sales team should suggest that there might be legal consequences if patients were not reviewed and alternative treatment options offered.

The Panel noted that despite the content of the email follow up summary from the RBM and one interviewee's impression, the remainder of the staff (five) at the February sales meeting were clearly concerned about the impression given by the RBM. The Panel was concerned that staff recalled phrases 'if you don't do this, you might be sued' and 'to make this message personal as their customers could be sued. Using lurasidone could reduce the risk'.

The Panel further noted the complainant's allegation that Sunovion used a named barrister to discuss medico-legal practice as a presentation and the regional manager cited this in a team meeting as the basis and implied authority to challenge customer's prescribing. The Panel noted that certain interviewees stated that the RBM referred to the barrister and instructed the team to engage him/her in customer meetings with the intention of making customers feel uncomfortable about their medico-legal position with regard to monitoring antipsychotics. It was also stated that the RBM said that 'if they do not offer a change of treatment and make a note of it, it could come back and bite them'. The barrister's presentation was mentioned by the RBM as a way of emphasising this point. Another interviewee stated that the RBM had been insistent about using the barrister to present at meetings 'in order to put pressure on customers'.

The Panel noted its comments above and considered that on the balance of probabilities the RBM had not maintained a high standard of ethical conduct and his/her verbal direction advocated a course of action

which would be likely to lead to a breach of the Code. Breaches of Clause 15.9 and 15.2 were ruled. There was no information about what Sunovion staff had said to health professionals etc. Therefore, the Panel considered that the complainant had not shown, on the balance of probabilities, that the representatives had not maintained a high standard of ethical conduct when promoting Latuda to health professionals etc, despite the RBM' briefing. No breach of Clause 15.2 of the Code was ruled in that regard.

The Panel further noted the complainant's allegation that the RBM had encouraged his/her staff to quote CQUIN measures that stated that a review of medication should be considered if a patient had side-effects. The Panel noted the complainant's concern that if such an approach was shared with customers it could bring the industry into disrepute. In the Panel's view, it was not necessarily unacceptable for companies to refer to CQUIN provided the manner in which it was done complied with the Code. The Panel noted that one interviewee stated that the RBM asked the team to use CQUIN as a tool to inform customers that they should consider switching treatment in patients with cardiovascular risk factors. It was not necessarily unacceptable under the Code for a company to promote a simple switch from one product to another. The Panel considered that the complainant had not shown, on the balance of probabilities that in referring to CQUIN the RBM's verbal direction advocated a course of action which would be likely to lead to a breach of the Code. No breach of Clause 15.9 was ruled in that regard. The Panel also ruled no breach of Clause 2 for similar reasons.

The Panel noted Sunovion's submission that referencing medico-legal consequences was not an acceptable approach to promote Latuda either directly or indirectly. The Panel noted its rulings above including that the complainant had not proved his/her complaint on the balance of probabilities in relation to the promotion to health professionals etc. In addition the Panel considered that its ruling of a breach of Clause 15.2 in relation to the RBM covered the position regarding high standards. The Panel ruled no breach of Clause 9.1. The company had not brought discredit upon or reduced confidence in the industry and therefore the Panel ruled no breach of Clause 2.

During the consideration of this case, the Panel was concerned to note that in its initial response Sunovion did not provide an accurate summary of the interviews carried out regarding the February sales meeting. This was only discovered when the Panel requested copies of the interviews conducted. The Panel queried why anonymised copies of these interviews had not been provided in the first instance. The Panel was disappointed by the conduct of Sunovion. Self-regulation relied, *inter alia*, upon the provision of complete and accurate information to the Panel.

In the Panel's view the barrister's presentation about the importance of informed patient choice appeared to be inconsistent with the company's submission that referencing medico-legal consequences was not an acceptable approach to promoting Latuda either directly or indirectly.

The Panel requested that Sunovion be advised of these concerns.

Sunovion provided the requisite undertaking and assurance and the Appeal Board received the case report as set out in Paragraph 13.4 of the Constitution and Procedure.

**APPEAL BOARD CONSIDERATION OF CASE REPORT**

The Appeal Board was very concerned to note that in its initial response to the Panel Sunovion did not provide an accurate summary of the interviews about the February sales meeting. This was only discovered when the Panel requested copies of the interviews conducted. The Appeal Board noted that self-regulation relied, *inter alia*, upon the provision of complete and accurate information but considered that the company's initial response was misleading. In that regard, the Appeal Board's view was that additional sanctions under Paragraph 11.1 of the Constitution and Procedure should be contemplated. Sunovion should respond to these concerns in writing and it was invited to appear before the Appeal Board when the matter was considered. Sunovion was provided with a copy of the papers.

**COMMENTS FROM SUNOVION**

Sunovion submitted that it was committed to full compliance with the Code and took its obligations very seriously. Sunovion had fully taken into account the Panel's findings and the Appeal Board's comments. Sunovion submitted that it had acted in good faith throughout the complaint process.

Sunovion noted that in response to Case AUTH/2850/6/16, it had provided a summary of interviews rather than submitting full interview transcripts with the initial response. Sunovion had followed that practice in relation to this complaint and did not know that this was an incorrect approach.

Sunovion submitted that it did not deliberately mislead the Panel in any way in relation to the February sales meeting. The summary of the interviews provided with the company's response to the complaint was a good faith attempt to set out the relevant facts. Sunovion did not try to hide any, or make any misleading comments about, the facts and it apologised if that impression had been given.

Sunovion submitted that it had always been prepared to cooperate fully and to provide any information that was requested. If Sunovion had known that the full interview transcripts were required with its initial response, they would have been provided.

In all the circumstances, and given that the company had fully taken everything on board, Sunovion submitted that any additional sanctions would be inappropriate and unwarranted.

At the consideration of this matter the Sunovion representatives stated that the company fully accepted the Panel's findings and took full responsibility for this matter. Sunovion had already briefed all employees on the learnings from the case and had planned additional training on the Code. Sunovion supported the Code and was committed to compliance, self-regulation and transparency.

Sunovion Pharmaceuticals Inc. was based in the US, UK and Canada, and its parent company, Sumitomo Dainippon Pharma Co., Ltd was based in Japan. Sunovion submitted that it had an extremely strong culture of compliance, ethics and business integrity supported by a comprehensive global compliance and ethics program. One of the senior executives of the parent company currently, and had previously, held office in the Japan Pharmaceutical Manufacturers Association (JPMA).

The Sunovion representatives stated that Sunovion's initial response to the complaint and summary of interviews was fact-based and made in good faith with no intent to mislead. Sunovion understood and accepted the Appeal Board's position that, given the standard of 'the balance of probabilities', the response could be viewed as misleading. Upon the PMCPA's request, Sunovion had promptly provided the interview notes.

In view of the helpful clarification and comments from the Panel and the Appeal Board, in the unlikely event of a future complaint, Sunovion would submit any interview notes with its initial response.

**APPEAL BOARD CONSIDERATION**

The Chairman noted that the Appeal Board now had before it the correspondence and submissions in relation to this case and Sunovion's response to the Appeal Board's consideration of the case report and Panel minute (received in accordance with Paragraph 4.1 of the Constitution and Procedure at its meeting in July).

The Appeal Board noted the Panel's rulings of breaches of Clauses 15.2 and 15.9 of the Code and that the company had apologised and admitted that it had made errors.

The Appeal Board noted that contrary to the written comments made by Sunovion in response to the concerns raised by the Appeal Board, the issue was that the summary was not a fair reflection of the interview transcripts, not that the transcripts had not been provided with the company's original response.

The Appeal Board asked the Sunovion representatives to explain how the interview transcripts from the six representatives could be summarised as giving a mixed and somewhat unclear impression of the verbal direction provided by the RBM when 5 of the 6 supported the complainant. This point had not been addressed by Sunovion.

The Appeal Board noted that in response to questioning the Sunovion representatives stated that the interviews were conducted by a senior UK director who was solely responsible for investigating this complaint. That director's findings were that although the picture was mixed and unclear there was a strong probability that the RBM had done something wrong and that, on the balance of probabilities, this was in breach of the Code. According to the company representatives, this was included in the initial draft of the company's response to the complaint which was sent to the US parent company. The US parent company decided, based on external legal advice that, in spite of self-regulation, it was not Sunovion's responsibility to prove the complaint. It altered the UK company's draft and denied breaches of the Code stating that the interviews provided a mixed and somewhat unclear impression of the verbal direction provided. When making the changes the US parent company had no sight of the interview transcripts. Before signing the amended draft of the company's response, a senior European executive requested sight of the interview transcripts. Sunovion's representatives stated that when the senior UK investigating director had been shown the revised draft and advised of the legal opinion from the US he/she still stood by his/her original draft. The Appeal Board noted that the senior European executive stated that he/she was not an expert on the Code.

The Appeal Board considered that the responses of the company representatives to its questions were entirely contrary to Sunovion's written submissions to both the Panel and the Appeal Board and to the company's submission at the consideration of this matter that the summary of the interviews provided with the company's response to the complaint was a good faith attempt to set out the relevant facts. The company's presentation also stated that Sunovion supported the Code, was committed to compliance, self-regulation and transparency.

The Appeal Board noted that the senior UK investigating director's findings had been undermined by the US parent company which had not even seen the interview transcripts. At the Appeal Board hearing the US parent company representative acknowledged that it had compromised the professional integrity of the senior European executive. It did not stand behind the letter today. The US parent company representative also stated that many lessons had been learned and apologised. The Appeal Board was extremely concerned about the company's explanation. It considered that such a deliberately inaccurate, misleading and disingenuous response brought discredit upon and reduced confidence in the pharmaceutical industry. Whilst it might not be the respondent company's responsibility to prove a breach of the Code, it was the respondent company's responsibility to provide accurate information. Self-regulation relied, *inter alia*, upon the provision of complete and accurate information from pharmaceutical companies. The Appeal Board noted the submissions from the Sunovion representatives and it considered that the company's conduct in altering its response, contrary to that of the investigator and the clear evidence from the interviews, raised very serious concerns about system failure and company culture.

The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, Sunovion should be publicly reprimanded for

providing inaccurate and misleading information to the Panel and Appeal Board. The Appeal Board also decided to require an audit of Sunovion's procedures in relation to the Code. The audit should include interviews with staff at the US and Japanese parent companies. The audit would take place in November 2017 and on receipt of the report the Appeal Board would consider whether further sanctions were necessary.

**APPEAL BOARD FURTHER CONSIDERATION**

Sunovion was audited in November 2017 and on receipt of the audit report in January 2018 the Appeal Board questioned how seriously the whole Sunovion organisation was taking its commitment to self-regulation. The culture with regard to the Code and leadership on compliance matters needed to urgently improve across the organisation. The company in the US, Sunovion Pharmaceuticals Inc, and in particular the parent company in Japan, Sumitomo Dainippon Pharma Co, needed to demonstrate that the seriousness of the situation was understood and appropriate action taken.

The Appeal Board noted that the audit report highlighted many issues and concerns to be addressed including arrangements for advisory boards, certification, updating and compliance with standard operating procedures, role of medical science liaison staff, control and updating of material and attention to detail and management of all third-party service providers. Significant commitment was required to address these issues.

On receipt of further information in February and March 2018, and on noting the dates for completion of some of the actions etc, the Appeal Board decided that the company should be re-audited in June 2018. On receipt of the report for the re-audit the Appeal Board would decide whether further sanctions were necessary.

Sunovion was re-audited in June 2018 and on receipt of the report of the re-audit in September 2018 the Appeal Board noted that Sunovion had made some meaningful progress and that there appeared to be a genuine wish to create a more sophisticated compliance infrastructure and to build on the improvements made. The Appeal Board noted that Sunovion had committed greater staff resource to help address its compliance needs. The Appeal Board welcomed the reported improved relationship between Sunovion and its US parent company.

The Appeal Board was again concerned about the inaccurate responses from the company with regard to its disclosure of payments to patient organisations at the re-audit and it noted the related issues that arose in Case AUTH/3027/3/18. It was paramount that Sunovion ensured its responses to the PMCPA were accurate.

The Appeal Board noted that the report of the re-audit still highlighted further important issues and concerns to be addressed including a review of its material, updating standard operating procedures, urgently address the company's apparent lack of understanding of the definition of promotion, review of the active materials list and further training. Significant ongoing commitment was required to address these issues.

The Appeal Board decided that Sunovion Pharmaceuticals Europe should be re-audited in April 2019. On receipt of the report of the re-audit the Appeal Board would decide whether further sanctions were necessary.

Sunovion was re-audited in April 2019 and on receipt of the report of the re-audit in July 2019 the Appeal Board noted that Sunovion Pharmaceuticals Europe had continued to build on the improvements described in the report of the June 2018 re-audit in Case AUTH/2935/5/17. Staff had spoken positively about the steps taken by Sunovion Pharmaceuticals Europe to improve its compliance infrastructure. Compliance was now the top priority for the global Japanese parent, Sumitomo Dainippon. Sunovion Pharmaceuticals Inc in the US accepted that Sunovion Pharmaceuticals Europe was the subject matter expert on the Code. It was noted that the general manager continued to give strong and consistent messages about the importance of compliance and that compliance was now part of everybody's objectives.

The Appeal Board noted that the re-audit report still highlighted concerns including with regard to updating standard operating procedures and policies.

The Appeal Board noted that there had been significant progress at Sunovion since the re-audit in June 2018. The Appeal Board noted that Sunovion had a compliance action plan to address recommendations from the re-audit. The Appeal Board noted some actions were already completed and that others were due to be completed very shortly. On the basis that this work was completed, the progress shown to date was continued and a company-wide commitment to compliance was maintained, the Appeal Board decided that no further action was required.

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| **Complaint received** | **13 February 2017** |
| **Undertaking received** | **19 June 2017** |
| **Appeal Board consideration** | **7 September 2017, 11 January, 7 February, 22 March 2018, 13 September, 11 July 2019** |
| **Interim case report first published** | **30 October 2017** |
| **Case completed** | **11 July 2019** |

CASE AUTH/2939/2/17 and AUTH/2940/2/17

# VOLUNTARY ADMISSION BY ASTELLAS UK AND ASTELLAS EUROPE

## Failure to provide accurate prescribing information

**Astellas UK and Astellas Europe respectively voluntarily admitted breaches of the Code with regard to the content of prescribing information for seven medicines promoted by Astellas in the UK.**

**Whilst the voluntary admission was made under the self-regulatory system, given the potential impact on patient safety, the companies informed the Medicines and Healthcare products Regulatory Agency (MHRA) which was advised that the PMCPA was dealing with the matter as a complaint under the Code.**

**As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Astellas. In addition to the clauses cited by Astellas, (Clauses 4.2, 9.1 and 2) the companies were also asked to consider the requirements of Clauses 4.1, 4.10 and 26.3 of the Code.**

**Astellas stated that the issues highlighted did not relate to the content of any summaries of product characteristics (SPC) or patient information leaflets (PIL).**

**Astellas UK provided detailed background information. In late November 2016, the copy approval system raised an alert that the prescribing information for Flomaxtra XL (tamsulosin hydrochloride) was due for routine re-approval. During the review process a signatory noticed that at least one adverse reaction contained within the Flomaxtra XL SPC (Stevens–Johnson syndrome) which should be categorised as serious had not thus far been included in the prescribing information.**

**The issue was initially thought to be isolated to the prescribing information for one medicine, omitting three serious adverse reactions (Stevens-Johnson syndrome, syncope and priapism).**

**However, a thorough investigation (as detailed below) identified the breadth of the issue, including the impact on Astellas Europe. Astellas Europe was informed of the issue in February 2017, and then began its own review (see below).**

**The review was conducted on all medicines currently promoted by Astellas UK, namely Advagraf, Betmiga, Dificlir, Modigraf, Mycamine, Prograf, Qutenza, Vesicare and Xtandi. The review also revealed that in addition to the inconsistent categorisation around seriousness, there were a number of incidences of common adverse reactions, as well as warnings and precautions, which had not been included in the prescribing information.**

**There had been inconsistency in ownership of the construction of the original prescribing information in Astellas UK. Where Astellas UK had documented the development of the original prescribing information through the Zinc approval system, these products (Betmiga, Xtandi, Dificlir and Qutenza) had been unaffected by the omissions described. For the affected products, it was unclear as to whether the original prescribing information was developed by Astellas UK.**

**However, the process for the approval of revised prescribing information had been erroneously confined to the review of the information that had been revised, rather than a full review of the prescribing information every time. Thus, if the prescribing information was incomplete from the outset, this was not picked up at subsequent revisions.**

**As an immediate action, the prescribing information and all promotional items for the Astellas medicines promoted that had incomplete prescribing information (Flomaxtra, Vesomni, Vesicare, Advagraf, Prograf, Modigraf and Mycamine) had been withdrawn. As an interim measure, the SPC would be used in the UK supplemented with the legal classification and the cost. This interim solution would remain in place until a revised process was in place.**

**Astellas Europe was the regional headquarters for Europe, Middle East and Africa (EMEA), based in the UK, and therefore operated differently to Astellas UK with regard to the creation of promotional material and use of prescribing information. Astellas Europe created regional template promotional materials for adaption according to local law or codes of practice ie materials would be reviewed and adapted for local use by the relevant affiliate.**

**There were some materials and activities that were produced and implemented by Astellas Europe directly. These generally used Astellas Europe generated/adapted prescribing information.**

**Under the current process for development and revision of UK prescribing information Astellas Europe, medical affairs had assumed responsibility for updating prescribing information when it became aware of SPC updates. Historically each brand team had taken a slightly different approach, and had either used the UK prescribing information as a basis and adapted that, together with a supplementary adverse event reporting statement, or prepared their own European/EMEA version of prescribing information.**

**Subsequent to the Astellas UK investigation, a review of prescribing information and promotional materials generated by Astellas Europe had been initiated.**

**Astellas Europe was notified of this issue in February 2017. It had no formal written process around the development and revision of prescribing information and had not routinely been notified about prescribing information updates. The same lack of guidance around categorisation of seriousness applied equally to Astellas Europe.**

**There had been no consistent approach to the approval process across brands and the process was not well defined. Astellas recognized that this needed to be, and was working to ensure that the process was, robust and consistent.**

**A review was undertaken of serious and common adverse events, contraindications, warnings and precautions in the active Astellas Europe prescribing information for Advagraf, Betmiga, Dificlir, Modigraf, Prograf, Qutenza, Vesomni, Vesicare and Xtandi. This review had identified omissions in the Astellas Europe prescribing information for Vesomni and Vesicare. An analysis of these omissions was provided.**

**There was no active Astellas Europe prescribing information for Mycamine.**

**A full retrospective analysis of Astellas Europe prescribing information was completed at the end of February. This showed omissions for previous versions of the prescribing information for Mycamine and Qutenza.**

**A review had been undertaken of all the active Astellas Europe promotional material for Advagraf, Betmiga, Dificlir, Modigraf, Mycamine, Prograf, Qutenza, Vesomni, Vesicare and Xtandi to identify if any materials needed to be recalled, the results of which were provided.**

**As an immediate action the active prescribing information for Vesomni and Vesicare and the identified promotional materials were recalled.**

**Astellas UK and Astellas Europe stated that it was clear that Astellas required a robust, consistent and reproducible process for the generation of prescribing information. A discussion with global colleagues had started and a cross-functional task force formed to work on a revised process.**

**The companies submitted that there were issues with the prescribing information for seven medicines. In addition, Astellas UK and Astellas Europe acknowledged that the deficiencies in their processes which related to the consistent inclusion of the relevant safety information in the prescribing information of these products represented a failure to maintain high standards. Given that such omissions had the potential to impact on patient safety, the companies considered the issues uncovered were contrary to the requirements of Clause 2 and in that regard they had sent a copy of the voluntary admission to the MHRA.**

**The companies submitted that they were treating this issue with the utmost seriousness; they recognized the gravity of the situation and were addressing it as a priority.**

**The detailed response from Astellas UK and Astellas Europe appears below.**

**The Panel was extremely concerned that incomplete prescribing information had been used by the companies for a number of years on large numbers of materials. It noted the companies' submissions that the omissions from the Astellas UK prescribing information included serious adverse reactions as well as common adverse reactions, warnings and precautions. The omissions from the Astellas Europe prescribing information included inconsistent categorisation around seriousness as well as common adverse reactions, warnings and precautions. The Panel was also very concerned that the systems at both companies had not picked up the errors sooner.**

**The Panel noted that both Astellas UK and Astellas Europe had withdrawn current materials with incomplete prescribing information. These being Astellas UK materials for Flomaxtra, Vesomni, Vesicare, Advagraf, Prograf, Modigraf and Mycamine. The Astellas Europe materials related to Vesomni and Vesicare. In addition Astellas Europe had identified omissions in previous versions of the prescribing information for Mycamine and Qutenza.**

**The Panel ruled breaches of the Code in relation to each of the seven Astellas UK products with incomplete prescribing information and in relation to each of the four Astellas Europe products with incomplete prescribing information. High standards had not been maintained and breaches of the Code were ruled. The Panel considered that the failures brought discredit upon and reduced confidence in the pharmaceutical industry. It was crucial that health professionals and others could rely completely upon the industry for up-to-date and accurate information about their medicines. Breaches of Clause 2 of the Code were ruled.**

**With regard to the use of the black triangle, the Panel accepted Astellas UK and Astellas Europe's submissions that the black triangle was not required to be included in the prescribing information and thus ruled no breaches of the Code.**

**The Panel was extremely concerned about its rulings and comments above. Some of the matters raised went to the heart of self-regulation and patient safety. Astellas' oversight of the prescribing information had been very poor. Notwithstanding the fact that Astellas UK was currently suspended from membership of the ABPI and already undergoing a series of audits of its procedures under the Code, the Panel decided, in accordance with Paragraph 8.2 of the Constitution and Procedure, to report both Astellas UK and Astellas Europe to the Appeal Board for it to consider whether further sanctions were appropriate in these cases.**

**The Appeal Board noted that these cases had arisen from a voluntary admission by Astellas UK and Astellas Europe and that the companies had**

**accepted all the rulings of breaches of the Code including Clause 2. The Appeal Board also noted that Astellas sincerely apologised for the failings.**

**The Appeal Board considered that these cases raised serious concerns about multiple failings and a complete lack of control. The lack of processes with regard to updating prescribing information was shocking. The Appeal Board considered the companies' failure to ensure that prescribing information was accurate and complete was totally unacceptable and that such failings raised very serious concerns with regard to patient safety. The Appeal Board considered that given the importance of patient safety, this issue should have been an absolute priority. The amount of time that had elapsed between Astellas UK discovering the problem (late November 2016) and completing a cross-check of SPCs against prescribing information (27 January 2017) was totally unacceptable. It appeared that Astellas Europe was not informed until late January and in early February Astellas Europe was updated with a list of products with prescribing information issues. The voluntary admissions were made in February. The Appeal Board did not consider that the explanation from Astellas including that neither Flomaxtra or Vesomni were actively promoted and therefore staff had not initially realised the seriousness of the situation and the difficulty of arranging meetings in December/ January justified the delay in taking appropriate action. In addition given the heightened focus on compliance arising from other issues faced by the companies, the Appeal Board considered that much greater priority should have been given to reviewing the materials and understanding the scale of the problems.**

**The Appeal Board noted that Astellas UK was currently suspended from membership of the ABPI in relation to matters arising in Case AUTH/2780/7/15. Astellas UK and Astellas Europe had each been audited in December 2015 and September 2016 and more recently in April 2017 which also covered the audit required in Case AUTH/2883/10/11.**
**The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, both companies should be publicly reprimanded for a lamentable lack of concern for patient safety and wholly inadequate oversight and control. The Appeal Board also decided to require an audit of both Astellas UK and Astellas Europe procedures in relation to the Code. The audits would take place in October 2017 and on receipt of the report, the Appeal Board would consider whether further sanctions were necessary.**

**The Appeal Board considered that these cases raised very serious matters due to the total failure of the companies' systems in relation to the control of prescribing information, the potential consequences for patient safety and the continuing nature of the failures over many years. In addition, given the level of scrutiny the companies were already under in relation to compliance, the Appeal Board was very concerned about the initial lack of urgency in conducting a full review and addressing any issues as set out above. Consequently, the Appeal Board decided that in accordance with Paragraph 12.1 of the Constitution and Procedure, both companies should be reported to the ABPI Board.**

**The ABPI Board noted the rulings of breaches of the Code in each case, the decisions of the Appeal Board regarding audits, and public reprimands in each case and that each case had been reported separately to the ABPI Board.**

**The ABPI Board noted and endorsed the Appeal Board's views about the total failure of the companies' systems in relation to the control of prescribing information, the lamentable lack of concern for patient safety, wholly inadequate oversight and control and initial lack of urgency. It was a woeful state of affairs.**

**The ABPI Board gave serious consideration to expelling Astellas UK from membership of the ABPI. However, it noted the commitments from Astellas Europe, the global company and of the new UK General Manager. The companies had made voluntary admissions and it was now imperative that the October re-audits showed significant progress.**

**The ABPI Board decided that it would extend the suspension of Astellas UK from membership of the ABPI for another 12 months. This further period would run uninterruptedly from the initial period of suspension and would then amount to the maximum suspension (two years) allowed under the ABPI Articles of Association.**

**The ABPI Board also decided that it wanted sight of the report of the October 2017 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of 2017. If the report of the re-audits did not show significant improvement and progress at both companies, then the ABPI Board would consider expelling Astellas UK from membership of the ABPI. The companies should consider undergoing an external assessment of progress, particularly in relation to risk management of compliance in the broadest sense, ie including matters beyond the scope of the Code, with the outcome to be available at the time of the October 2017 re-audits.**

**The ABPI Board also decided that the MHRA should be advised of the ABPI Board's very serious concerns about the conduct of Astellas UK and Astellas Europe particularly in relation to the matters concerning patient safety. EFPIA should also be updated and asked to ensure the EFPIA Board was informed of the position.**

**Astellas UK and Astellas Europe were re-audited in October 2017 and the report of the re-audit was considered in November. The Appeal Board noted that as these were the fourth audits of the companies and given that Astellas UK was currently suspended from membership of the ABPI, it expected substantial progress and improvements from both companies. This expectation had not been met. The Appeal Board acknowledged that some progress had been made. The companies must**

**take prompt action to implement the findings and recommendations in the report of the October 2017 re-audits.**

**The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been positive changes in the company culture. However, it was not convinced that the expected progress was being made, especially since the April 2017 re-audits.**

**Overall, the Appeal Board's view was that the rate of progress was inadequate and that the companies were not where they should be. There was still much work to do. The Appeal Board queried whether there was an element of structural inertia or perhaps fear of wrongdoing which was inhibiting or slowing the rate of progress.**

**Despite its criticisms, the Appeal Board noted the positive steps taken by the leadership of Astellas to engage more broadly with staff and drive changes.**

**The Appeal Board decided that both companies should be re-audited in April 2018. At which point it expected the 2018 global staff survey to demonstrate improvements at Astellas Europe and Astellas UK.**

**Whilst noting that this was entirely a matter for the ABPI Board, the Appeal Board's view was that if the report of the October 2017 re-audits and Astellas' response had come at the end of the two year suspension limit, then Astellas would have fallen well short of the standard required to resume membership of the ABPI. Unless substantial progress was seen in the report of the re-audits in April 2018, in the Appeal Board's view, Astellas UK would be at serious risk of a recommendation that it be expelled from membership of the ABPI.**

**The ABPI Board noted the Appeal Board's comments and concerns about the re-audits in October 2017 and the additional information provided by Astellas.**

**With regard to the external assessment of progress, particularly in relation to risk management of compliance in the broadest sense ie including matters beyond the scope of the Code, the ABPI Board noted the information provided by Astellas.**

**Following a change in tone from the top of Astellas, the ABPI Board recognised that meaningful progress had been made by the companies. The ABPI Board understood the difficulty inherent in making wide-sweeping cultural changes, and how long it took for those changes to become fully embedded within a large organisation. However, the ABPI Board acknowledged Astellas' clear commitment to further improvement.**

**The ABPI Board noted Astellas' statement that its materials were compliant in May 2017 in relation to issues of patient safety.**

**The ABPI Board also decided that it wanted sight of the report of the April 2018 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of the current suspension in June 2018.**

**The ABPI Board decided that taking all the circumstances into account it would take no further action at this stage in relation to the expulsion of Astellas from membership of the ABPI. The suspension from membership of the ABPI would remain in place until June 2018.**

**The ABPI Board also decided that the MHRA should be advised of the position. EFPIA should also be updated and asked to ensure that the EFPIA Board was informed of the position.**

**Astellas UK and Astellas Europe were re-audited in April 2018 and the report of the re-audits was considered in May 2018.**

**The Appeal Board noted the detailed responses from Astellas to the report of the April 2018 re-audits including that it was an accurate reflection of the work undertaken.**

**The Appeal Board noted the results of the 2018 staff survey and the progress made. Numerical increases had been shown in a number of parameters since the previous survey in July 2017. There were concerns about the comments made by staff. The Appeal Board also noted the differences in the Astellas UK results which were generally better than the Astellas Europe results. The Appeal Board considered that the Astellas Europe management committee scores although improved were still not where they should be.**

**The Appeal Board noted the comments in the report of the April 2018 re-audits and considered that both the leadership of Astellas Europe and Astellas UK had engaged with staff to bring about progress. There was still work to be done. The Appeal Board noted one of the recommendations was that members of the leadership team at Astellas Europe should be held to account and be challenged on compliance matters.**

**The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been further positive changes in the company culture and this needed to be continued. The Appeal Board noted that there had been some positive compliance initiatives. The discussion fora and communications continued and progress had been made including ensuring staff had time to complete training.**

**The Appeal Board noted that whilst as a percentage there had been a significant increase the number of job bags, the overall numbers was still low. As Astellas increased its activities it must remain extremely vigilant to compliance requirements in particular in relation to certain higher risk activities such as patient support programmes, product launches etc. The true test of the compliance framework in Astellas and its approach would be when activity levels including higher risk activities were increased and the company was operating at business as usual.**

**The Appeal Board considered that, at long last, the re-audits in April 2018 showed that progress had been made and that the companies were building**

**on momentum started in summer 2017. The Appeal Board was concerned that these were the fifth audits of each company and that the first audits were in December 2015. It was extraordinary that it had taken so long to demonstrate meaningful change. The overall impression from the report of the April 2018 re-audits was that Astellas was showing improvement and momentum. However, whilst the companies had reached a certain level, given all the circumstances including that Astellas UK had been suspended from membership of the ABPI and that the Appeal Board still had concerns, the Appeal Board decided that Astellas Europe and Astellas UK should each be re-audited at the end of the first quarter of 2019 to ensure that the improvements and the momentum continued and were built upon.**

**On the information before it, and noting that Astellas UK was still to respond to the PMCPA in relation to matters raised following completion of the consideration of a complaint concerning Astellas UK, Case AUTH/2984/10/17, the Appeal Board decided that sufficient progress had been made by the companies such that the Appeal Board did not consider that it warranted a recommendation for the expulsion of Astellas UK from membership of the ABPI when the matter came before the ABPI Board on 5 June 2018.**

**In June 2018 the ABPI Board noted the comments from both the Appeal Board and Astellas.**

**The ABPI Board noted the limited information provided about matters raised in Case AUTH/2984/10/17. This was still to be considered by the PMCPA and the Appeal Board and was not before the ABPI Board for consideration.**

**The view of the Appeal Board was clear. The ABPI Board agreed with the Appeal Board's views and assessment of the re-audits and concluded that meaningful progress had now been made.**

**The ABPI Board believed that the culture in the companies had improved and noted that much of this had been led by the General Manager of Astellas UK. However, the Board recognised the importance of an ongoing commitment to ensure sustained culture change. On reviewing all the material, the ABPI Board had concerns about the sustainability of the changes made given that there had already been five audits/re-audits, and especially as further types of activity were still to be fully re-introduced across the companies.**

**The ABPI Board therefore decided that it wanted to see the report of the 2019 re-audits and be informed of major developments including the outcome of Case AUTH/2984/10/17.**

**In the circumstances, there was no need for the ABPI Board to consider expelling Astellas UK from membership of the ABPI. The suspension would end on 24 June 2018 and Astellas would revert to full membership of the ABPI.**

**The ABPI Board also decided that the MHRA should be advised of the position and that EFPIA should be updated and asked to ensure that the EFPIA Board was informed of the position.**

**Astellas UK and Astellas Europe were re-audited in April 2019 and the report of the re-audits was considered in May 2019.**

**The Appeal Board noted the detailed response from Astellas Europe and Astellas UK to the report of the April 2019 re-audits.**

**The Appeal Board noted two new senior appointments; a new President EMEA Operations who joined Astellas in July 2018 and a new General Manager, Astellas UK who was appointed from April 2019.**

**The Appeal Board noted from the report of the April 2019 re-audits that it appeared that a more compliant culture was embedded within Astellas with improved communication. It was essential that this was maintained.**

**The Appeal Board considered that Astellas UK must ensure a proper professional approach to investigating and responding to any complaint under the Code such that the shortcomings in Case AUTH/2984/10/17 were not repeated. The Appeal Board noted that an audit had not been required in Case AUTH/2984/10/17. The case had, in accordance with established practice, been discussed as part of an examination of the company's culture at the re-audits.**

**The Appeal Board noted that these were the sixth audits/re-audits of each company and that the first audits were in December 2015. The Appeal Board considered that, on the information provided in the report of the April 2019 re-audits, it appeared that the companies had made further improvements, that this would be maintained and broadly the companies were where they should be. The Appeal Board, however, remained very concerned about the amount of time it had taken Astellas to reach this point. The Appeal Board noted that Astellas stated that it would follow up on the issues identified in the report of the April 2019 re-audits and it was committed to maintaining its approach to embedding a sustainable compliance culture. The Appeal Board noted a number of activities/actions were due to be undertaken. On the understanding that this work was completed, that the progress shown to date was continued and a company-wide commitment to compliance was maintained, the Appeal Board decided that, on the basis of the information in the report of April 2019 re-audits, no further action was required in relation to Case AUTH/2780/7/15, Case AUTH/2883/10/16, Cases AUTH/2939/2/17 and AUTH/2940/2/17.**

**The Appeal Board noted that the audit/re-audits in these four cases had been required by the Appeal Board. They had not been required by the ABPI Board. Nonetheless, the Appeal Board noted the ABPI Board's request to see the report of the April 2019 re-audits.**

**At the re-audits in April 2019 it was noted that the MHRA decided that Astellas advertising materials should be submitted for review. This was introduced for all new materials issued since 1 December 2018.**

**In June 2019 the ABPI Board received an update as requested. It noted the comments from both the Appeal Board and Astellas and the improvements made.**

In Cases AUTH/2939/2/17 and AUTH/2940/2/17 Astellas UK and Astellas Europe respectively voluntarily admitted breaches of the Code with regard to the content of prescribing information for seven medicines promoted by Astellas in the UK. Astellas UK stated that the issue had the potential to impact certain Astellas Europe activities hence the joint voluntary admission.

Whilst the voluntary admission was made under the self-regulatory system, given the potential impact on patient safety, the companies had copied the letter to the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA was informed that the PMCPA was dealing with the matter as a complaint under the Code.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Astellas. In addition to the clauses cited by Astellas, (Clauses 4.2, 9.1 and 2) the companies were also asked to consider the requirements of Clauses 4.1, 4.10 and 26.3 of the Code.

**VOLUNTARY ADMISSION**

Astellas stated that the issues highlighted related to prescribing information only, and not to the content of any summaries of product characteristics (SPC) or patient information leaflets (PIL) for any Astellas medicine.

**Astellas UK**

**Background**

Astellas UK stated that in late November 2016, the Zinc copy approval system raised an alert that the prescribing information for Flomaxtra XL (tamsulosin hydrochloride) was due for routine re-approval. During the review process, and taking account of the requirements of Clause 4.2 of the Code (which required 'a succinct statement of common adverse reactions….serious adverse reactions…'), one of Astellas UK's medical signatories noticed that at least one adverse reaction contained within the Flomaxtra XL SPC (Stevens–Johnson syndrome) which should be categorised as serious had not thus far been included in the prescribing information.

The issue was initially thought to be isolated to the prescribing information for one medicine, omitting three serious adverse reactions (Stevens-Johnson syndrome, syncope and priapism).

However, a thorough investigation conducted in December 2016 and January 2017 (as detailed below) identified the breadth of the issue, including the impact on Astellas Europe. Astellas Europe was informed of the issue in February 2017, at which point it began its own review (see below).

**Current process for development and revision of UK prescribing information**

Astellas UK standard operating procedure (SOP) 1000, Control of New and Changed Products, covered the process up to and including the circulation of an approved SPC following a new product launch or update of the SPC following a variation. Once the approved SPC had been circulated by the Astellas UK regulatory team, the Astellas UK medical information department was responsible for constructing or revising the prescribing information and submitting this to the relevant Astellas UK medical affairs and/or commercial teams for review and approval in Zinc.

The MedInfo Manual entitled 'How to write Prescribing Information M16' (effective February 2014) was used to support the development and updating of prescribing information. Prior to this, there was no formal guidance on how to develop prescribing information, other than the requirements listed in Clause 4.2. The MedInfo Manual M16 did not provide guidance on how to categorise adverse reactions as serious.

**Investigation**

The companies stated that the SPCs listed side effects in accordance with their reported frequency and not with regard to their seriousness. For the purposes of this investigation, and in order to carry out a wider look at seriousness categorisation for adverse reactions in the SPCs, and hence their inclusion in the prescribing information, it was agreed with Astellas Global Pharmacovigilance colleagues that the EudraVigilance Expert Working Group publication entitled Important Medical Event Terms List (IME list), based on MedDRA version 19.1 would be the reference document. The review was conducted on all Astellas medicines currently promoted by Astellas UK, namely Advagraf, Betmiga, Dificlir, Modigraf, Mycamine, Prograf, Qutenza, Vesicare and Xtandi. The review also revealed that in addition to the inconsistent categorisation around seriousness, there were a number of incidences of common adverse reactions, as well as warnings and precautions, which had not been included in the prescribing information.

It became clear during the review that there had been inconsistency in ownership of the construction of the original prescribing information in Astellas UK. In those circumstances where Astellas UK had documented the development of the original prescribing information through the Zinc approval system, these products (Betmiga, Xtandi, Dificlir and Qutenza) had been unaffected by the omissions described. For the affected products, it was unclear as to whether the original prescribing information was developed by Astellas UK.

However, the process for the approval of revised prescribing information had been erroneously

confined to the review of the information that had been revised, rather than incorporating a full review of the prescribing information every time. Thus, if the prescribing information was incomplete from the outset, this was not picked up at subsequent revisions.

**Corrective action**

As an immediate action, the prescribing information and all promotional items for the Astellas medicines promoted that had incomplete prescribing information (Flomaxtra, Vesomni, Vesicare, Advagraf, Prograf, Modigraf and Mycamine) had been withdrawn. As an interim measure, the SPC would be used in the UK in lieu of Clause 4.2 (i) to (viii), supplemented with the legal classification and the cost. This interim solution would remain in place until a revised process for the development, approval and subsequent revision of prescribing information was drafted and implemented, to include a thorough review of prescribing information from the outset as well as at every revision; guidance on categorisation of adverse reactions would also be included.

**Astellas Europe**

**Background**

Astellas Europe was the regional headquarters for Europe, Middle East and Africa (EMEA), based in the UK, and therefore operated differently to Astellas UK with regards to the creation of promotional material and use of prescribing information. Astellas Europe created regional template promotional materials for adaption according to local law or codes of practice ie materials would be reviewed and adapted for local use by the relevant affiliate eg Astellas UK in the UK.

There were some materials and activities that were produced and implemented by Astellas Europe directly ie not executed locally by affiliates. These included congress symposia, congress booths, pan-European stand-alone meetings and journal advertisements/supplements. These used Astellas Europe generated/adapted prescribing information as outlined below, unless local rules necessitated otherwise eg stricter rules might apply in a country where a congress was held, or where a journal advertisement or supplement was published.

**Current process for development and revision of UK prescribing information**

Astellas Europe, medical affairs had assumed responsibility for updating prescribing information when it became aware of SPC updates. Historically each brand team had taken a slightly different approach, and had either used the UK prescribing information as a basis and adapted that, together with a supplementary adverse event reporting statement, or prepared their own European/EMEA version of prescribing information.

Subsequent to the Astellas UK investigation, a review of prescribing information and promotional materials generated by Astellas Europe had been initiated (see below).

Astellas Europe was notified of this issue in February 2017. It had a supportive tool (STL-1793 and parent document SOP 256 Review and Approval of Materials or Activities (Zinc)), which outlined the requirements for prescribing information at an EMEA regional headquarters level.

Astellas Europe had no formal written process around the development and revision of prescribing information and had not routinely been notified about prescribing information updates. The same lack of guidance around categorisation of seriousness applied equally to Astellas Europe.

There had been no consistent approach to the approval process across brands and the process was not well defined. Astellas recognized that this needed to be, and was working to ensure that the process was, robust and consistent.

**Investigation**

A review was undertaken of serious and common adverse events, contraindications, warnings and precautions in the active Astellas Europe prescribing information for Advagraf, Betmiga, Dificlir, Modigraf, Prograf, Qutenza, Vesomni, Vesicare and Xtandi. This review had identified omissions in the Astellas Europe prescribing information for Vesomni and Vesicare. An analysis of these omissions was provided.

There was no active Astellas Europe prescribing information for Mycamine. There were no omissions with respect to serious and common adverse events, contraindications, warnings and precautions in the active Astellas Europe prescribing information for Advagraf, Betmiga, Dificlir, Modigraf, Prograf, Qutenza, and Xtandi.

For completeness, a full retrospective analysis of Astellas Europe prescribing information was underway to be completed by the end of February.

A review had been undertaken of all the active Astellas Europe promotional material for Advagraf, Betmiga, Dificlir, Modigraf, Mycamine, Prograf, Qutenza, Vesomni, Vesicare and Xtandi to identify if any materials needed to be recalled, the results of which were provided.

As an immediate action the active prescribing information for Vesomni and Vesicare and the identified promotional materials were recalled (initiated on 20 February 2017 completed by 24 February 2017).

**Astellas UK and Astellas Europe**

**Preventative action**

The companies submitted that it was clear that Astellas required a robust, consistent and reproducible process for the generation of prescribing information in accordance with the Code. This involved a collaborative approach with global colleagues. This discussion had already started and a cross-functional task force formed to work on a revised process.

**Code Clauses**

The companies submitted that there had been seven breaches of Clause 4.2 (there were issues with the prescribing information for seven medicines). In addition, Astellas UK and Astellas Europe acknowledged that the deficiencies in their processes which related to the consistent inclusion of the relevant safety information in the prescribing information of these products represented a failure to maintain high standards, in breach of Clause 9.1. Given that such omissions had the potential to impact patient safety, the companies considered the issues uncovered were contrary to the requirements of Clause 2 and in that regard they had sent a copy of the voluntary admission to the MHRA.

The companies submitted that they were treating this issue with the utmost seriousness; they recognized the gravity of the situation that had been uncovered by the investigation and were addressing it as a priority.

**RESPONSE ASTELLAS UK**

Astellas UK pointed out that it only implemented the use of Zinc for approval of material in 2009, therefore the lists of the revisions to prescribing information and certificates and the lists of materials effected and withdrawn only went back as far as that date.

In relation to the products that were unaffected by the issue of incomplete prescribing information (Betmiga, Xtandi, Dificlir and Qutenza), Astellas UK submitted it was confident that there were no serious or common adverse events missing from the relevant prescribing information and that precautions and warnings reflected the substance of the relevant SPC. Although Qutenza was approved on 15 May 2009, its first marketing/commercial launch occurred only on 15 June 2010 and thus no prescribing information was produced in 2009.

As outlined above, Astellas UK submitted that there had been seven breaches of Clause 4.2 (there were issues with the prescribing information for seven medicines). The company understood that if prescribing information failed to meet the requirements of Clause 4.2 it was ruled in breach of Clause 4.1. Therefore Astellas UK considered there had been multiple breaches of Clause 4.1. In addition, the company acknowledged that the deficiencies in its process which related to the consistent inclusion of the relevant safety information in the prescribing information of its products represented a failure to maintain high standards, in breach of Clause 9.1. Given that such omissions had the potential to impact on patient safety, the issues uncovered were contrary to the requirements of Clause 2. Astellas UK had no further comment with regard to Clauses 4.2, 9.1 and 2, to add to those above.

With regard to Clauses 4.10 and 26.3 and the Authority's view that these clauses were relevant as the Astellas UK review of prescribing information noted a failure to include an inverted black triangle, Astellas UK routinely placed the black triangle on the prescribing information for products where additional monitoring was required. However, the inverted black triangle was also placed adjacent to the most prominent display of the product name. Therefore Astellas UK submitted there was no breach of either Clauses 4.10 or 26.3 if the black triangle was omitted from the prescribing information.

**RESPONSE ASTELLAS EUROPE**

The initial review undertaken by Astellas Europe focused on serious and common adverse events, contraindications, warnings and precautions in the active Astellas Europe prescribing information for Advagraf, Betmiga, Dificlir, Modigraf, Prograf, Qutenza, Vesomni, Vesicare and Xtandi. This review identified omissions in the Astellas Europe prescribing information for Vesomni and Vesicare. An analysis of these two products was then expanded retrospectively and provided previously.

A wider retrospective analysis had now been conducted by Astellas Europe on the UK licensed products promoted by Astellas Europe, namely Advagraf, Betmiga, Dificlir, Modigraf, Mycamine, Prograf, Qutenza, Vesicare and Xtandi. The review of prescribing information focused on serious and common adverse events, contraindications and warnings and precautions, but not the inclusion of the black triangle. The presence of an inverted black triangle on prescribing information was not a requirement of the Code *per se* (the Code required that promotional material and product related material for patients contained a black triangle).

The result of the Astellas Europe retrospective review was provided. The prescribing information was mainly generated on a needs basis as it was usually used for one-off congress items. The retrospective analysis for each product was conducted by the individual brand teams to ensure the history behind each update could be included in the spreadsheet.

The review revealed that in addition to the inconsistent categorisation around seriousness, there were a number of incidences of common adverse reactions, as well as warnings and precautions, which had not been included in the prescribing information.

This retrospective review identified omissions in the Astellas Europe prescribing information for Vesomni, Vesicare, Mycamine and Qutenza at various stages of their lifecycle:

- An analysis of the omissions for Vesomni and Vesicare was provided previously and was included as part of the full analysis below.
- There was no active Astellas Europe prescribing information for Mycamine but retrospective review showed there were earlier omissions in the prescribing information.
- Whilst no omissions were seen in the active Astellas Europe prescribing information for Qutenza, the retrospective review showed earlier omissions in the prescribing information.
- There were no omissions with respect to serious and common adverse events, contraindications,

warnings and precautions in the active and retrospective Astellas Europe prescribing information for Advagraf, Betmiga, Dificlir, Modigraf, Prograf, and Xtandi.

As an immediate action the active prescribing information for Vesomni and Vesicare was recalled as notified in the voluntary admission.

Astellas Europe noted that it only implemented the use of Zinc for approval of material in 2010, therefore the revisions to the prescribing information, lists of material effected (those produced by Astellas Europe directly ie, not executed locally by affiliates) and the lists of Astellas Europe materials withdrawn only went back as far as then.

As outlined above, Astellas Europe submitted that there had been four breaches of Clause 4.2 (there were issues with the prescribing information for four medicines). The company understood that if prescribing information failed to meet the requirements of Clause 4.2 it was ruled in breach of Clause 4.1. Therefore, Astellas Europe considered that there had been multiple breaches of Clause 4.1. In addition, the company acknowledged that the deficiencies in its process which related to the consistent inclusion of the relevant safety information in the prescribing information of the products represented a failure to maintain high standards, in breach of Clause 9.1. Given that such omissions had the potential to impact on patient safety, the issues uncovered were contrary to the requirements of Clause 2.

With regard to Clauses 4.10 and 26.3 and the Authority's view that these clauses were relevant as the Astellas Europe review of prescribing information noted a failure to include an inverted black triangle, Astellas Europe stated it was aware of the requirement to place it adjacent to the most prominent display of the product name. Therefore Astellas Europe submitted there was no breach of either Clause 4.10 or 26.3 if the black triangle was omitted from the prescribing information.

**PANEL RULING**

The Panel was extremely concerned that incomplete prescribing information had been used by the companies for a number of years. It noted the companies' submissions that the omissions from the Astellas UK prescribing information included serious adverse reactions as well as common adverse reactions, warnings and precautions. The omissions from the Astellas Europe prescribing information included inconsistent categorisation around seriousness as well as common adverse reactions, warnings and precautions. The Panel was also very concerned that the systems at both companies had not picked up the errors sooner.

The Panel noted that both Astellas UK and Astellas Europe had withdrawn current materials with incomplete prescribing information. These being Astellas UK materials for Flomaxtra, Vesomni, Vesicare, Advagraf, Prograf, Modigraf and Mycamine. The Astellas Europe materials related to Vesomni and Vesicare. In addition Astellas Europe had identified omissions in previous versions of the prescribing information for Mycamine and Qutenza.

The Panel was also concerned that large numbers of materials with incomplete prescribing information had been used for a number of years.

**Case AUTH/2939/2/17 Astellas UK**

The Panel ruled breaches of Clause 4.1 in relation to each of the seven Astellas UK products with incomplete prescribing information. High standards had not been maintained and a breach of Clause 9.1 was ruled. The Panel considered that the failures brought discredit upon and reduced confidence in the pharmaceutical industry. It was crucial that health professionals and others could rely completely upon the industry for up-to-date and accurate information about their medicines. A breach of Clause 2 was ruled.

With regard to the use of the black triangle, the Panel noted Astellas UK's submission that in addition to the requirements of the Code regarding the placing of the black triangle on promotional material (Clause 4.10) and information to the public (Clause 26.3) it routinely placed the black triangle on the prescribing information for products where additional monitoring was required. The company submitted that it was the additional black triangle on the prescribing information that had been omitted and which was highlighted in the company's review. The Panel noted that Astellas UK denied a breach of Clauses 4.10 and 26.3. The Panel accepted Astellas UK's submission in relation to the omission and thus ruled no breach of Clauses 4.10 and 26.3.

**Case AUTH/2940/2/17 Astellas Europe**

The Panel ruled breaches of Clause 4.1 in relation to each of the four Astellas Europe products with incomplete prescribing information. High standards had not been maintained and a breach of Clause 9.1 was ruled. The Panel considered that the failures brought discredit upon and reduced confidence in the pharmaceutical industry. It was crucial that health professionals and others could rely completely upon the industry for up-to-date and accurate information about their medicines. A breach of Clause 2 was ruled.

The Panel noted that Astellas Europe pointed out that it was not a breach of Clauses 4.10 and 26.3 if the black triangle was omitted from the prescribing information. The Panel accepted Astellas Europe's submission and thus ruled no breach of Clauses 4.10 and 26.3.

The Panel was extremely concerned about its rulings and comments above. Some of the matters raised went to the heart of self-regulation and patient safety. The company's oversight of the prescribing information had been very poor. Notwithstanding the fact that Astellas UK was currently suspended from membership of the ABPI and already undergoing a series of audits of its procedures under the Code, the Panel decided, in accordance with Paragraph 8.2 of the Constitution and Procedure,

to report both Astellas UK and Astellas Europe to the Appeal Board for it to consider whether further sanctions were appropriate.

**COMMENTS FROM ASTELLAS UK AND ASTELLAS EUROPE ON THE REPORT FROM THE PANEL**

Astellas UK and Astellas Europe fully accepted and agreed with all of the Panel's rulings. The companies were extremely disappointed to be in such a position. This was the second time in a short period of time that Astellas had been found in breach of the Code in relation to issues that might impact patient safety. The companies sincerely apologised for the failures highlighted. The companies noted the Panel's comments that their oversight of prescribing information had been poor and that some of the matters in this case went to the heart of self-regulation and patient safety. Both companies were committed to take all necessary action to raise their standards to address these matters.

Astellas had now initiated an assessment of processes relevant to the updating of prescribing information following the issue of, or change to, an SPC in all affiliates across the EMEA region.

Astellas Pharma Europe provided a report by its solicitors who carried out investigations into the recent voluntary admissions.

At the consideration of the report the representatives from Astellas UK and Astellas Europe stated that they sincerely apologised for the issues that led to these cases. The companies were extremely disappointed to be in this position; both organisations had worked very hard to address issues in relation to the companies' culture and processes during the last 12 months but clearly these cases had set them back significantly.

Astellas submitted that patient safety was a priority and it recognised that it was completely unacceptable to put this at risk. Astellas had initiated a review and validation of all processes relevant to the updating of prescribing information following the issue of, or change to, an SPC. In addition, Astellas had started new projects to improve 'third party vendor management' as well as 'patient support programmes' within its existing corrective and preventative action (CAPA) work streams. The objective was to put in place a robust and consistent process to ensure compliance with all relevant internal and external standards. Astellas was committed to achieve this as its first priority.

**APPEAL BOARD CONSIDERATION OF THE REPORT FROM THE PANEL**

The Appeal Board noted that these cases had arisen from a voluntary admission by Astellas UK and Astellas Europe and that the companies had accepted all the rulings of breaches of the Code including Clause 2. The Appeal Board also noted that Astellas sincerely apologised for the failings. However, the Appeal Board noted the Panel's comments and rulings above.

The Appeal Board considered that these cases raised serious concerns about multiple failings and a complete lack of control. The lack of processes with regard to updating prescribing information was shocking. The Appeal Board considered the companies' failure to ensure that prescribing information was accurate and complete was totally unacceptable and that such failings raised very serious concerns with regard to patient safety. The Appeal Board considered that given the importance of patient safety, this issue should have been an absolute priority. The amount of time that had elapsed between Astellas UK discovering the problem (which according to the solicitor's report was late November 2016) and completing a cross-check of SPCs against prescribing information (27 January 2017) was totally unacceptable. It appeared that Astellas Europe was not informed until late January and in early February Astellas Europe was updated with a list of products with prescribing information issues. The voluntary admissions were made in February. The Appeal Board did not consider that the explanation from the Astellas representatives including that neither Flomaxtra or Vesomni were actively promoted and therefore staff had not initially realised the seriousness of the situation and the difficulty of arranging meetings in December/January justified the delay in taking appropriate action. In addition given the heightened focus on compliance arising from other issues faced by the companies, the Appeal Board considered that much greater priority should have been given to reviewing the materials and understanding the scale of the problems.

The Appeal Board noted that Astellas UK was currently suspended from membership of the ABPI in relation to matters arising in Case AUTH/2780/7/15. Astellas UK and Astellas Europe had each been audited in December 2015 and September 2016 and more recently in April 2017 which also covered the audit required in Case AUTH/2883/10/11.

The Appeal Board noted that it had to consider the reports and whether to impose additional sanctions in Cases AUTH/2939/2/17 and AUTH/2940/2/17, on the evidence before it and independently of the other matters involving Astellas. The report of the April 2017 re-audits was to be considered by the Appeal Board shortly and by the ABPI Board in June 2017 when it would review the suspension of Astellas UK from membership of the ABPI.

The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, both companies should be publicly reprimanded for a lamentable lack of concern for patient safety and wholly inadequate oversight and control. The Appeal Board also decided to require an audit of both Astellas UK and Astellas Europe procedures in relation to the Code. The audits would take place in October 2017 and on receipt of the report, the Appeal Board would consider whether further sanctions were necessary.

The Appeal Board considered that these cases raised very serious matters due to the total failure of the companies' systems in relation to the control of prescribing information, the potential consequences for patient safety and the continuing nature of the failures over many years. In addition, given the

level of scrutiny the companies were already under in relation to compliance, the Appeal Board was very concerned about the initial lack of urgency in conducting a full review and addressing any issues as set out above. Consequently, the Appeal Board decided that in accordance with Paragraph 12.1 of the Constitution and Procedure, both companies should be reported to the ABPI Board.

**ABPI BOARD CONSIDERATION OF THE REPORT FROM THE APPEAL BOARD**

The ABPI Board noted the rulings of breaches of the Code in each case, the decisions of the Appeal Board regarding audits, and public reprimands in each case and that each case had been reported separately to the ABPI Board.

The ABPI Board noted and endorsed the Appeal Board's views about the total failure of the companies' systems in relation to the control of prescribing information, the lamentable lack of concern for patient safety, wholly inadequate oversight and control and initial lack of urgency. It was a woeful state of affairs.

The ABPI Board gave serious consideration to expelling Astellas UK from membership of the ABPI. However, it noted the commitments from Astellas Europe, the global company and of the new UK General Manager. The companies had made voluntary admissions and it was now imperative that the October re-audits showed significant progress.

The ABPI Board decided that it would extend the suspension of Astellas UK from membership of the ABPI for another 12 months. This further period would run uninterruptedly from the initial period of suspension and would then amount to the maximum suspension (two years) allowed under the ABPI Articles of Association.

The ABPI Board also decided that it wanted sight of the report of the October 2017 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of 2017. If the report of the re-audits did not show significant improvement and progress at both companies, then the ABPI Board would consider expelling Astellas UK from membership of the ABPI. The companies should consider undergoing an external assessment of progress, particularly in relation to risk management of compliance in the broadest sense, ie including matters beyond the scope of the Code, with the outcome to be available at the time of the October 2017 re-audits.

The ABPI Board also decided that the MHRA should be advised of the ABPI Board's very serious concerns about the conduct of Astellas UK and Astellas Europe particularly in relation to the matters concerning patient safety. EFPIA should also be updated and asked to ensure the EFPIA Board was informed of the position.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in October 2017 and the report of the re-audit was considered in November. The Appeal Board noted that as these were the fourth audits of the companies and given that Astellas UK was currently suspended from membership of the ABPI, it expected substantial progress and improvements from both companies. This expectation had not been met. The Appeal Board acknowledged that some progress had been made. The companies must take prompt action to implement the findings and recommendations in the report of the October 2017 re-audits.

The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been positive changes in the company culture. However, it was not convinced that the expected progress was being made, especially since the April 2017 re-audits.

Overall, the Appeal Board's view was that the rate of progress was inadequate and that the companies were not where they should be. There was still much work to do. The Appeal Board queried whether there was an element of structural inertia or perhaps fear of wrongdoing which was inhibiting or slowing the rate of progress.

Despite its criticisms, the Appeal Board noted the positive steps taken by the leadership of Astellas to engage more broadly with staff and drive changes.

The Appeal Board decided that both companies should be re-audited in April 2018. At which point it expected the 2018 global staff survey to demonstrate improvements at Astellas Europe and Astellas UK.

Whilst noting that this was entirely a matter for the ABPI Board, the Appeal Board's view was that if the report of the October 2017 re-audits and Astellas' response had come at the end of the two year suspension limit, then Astellas would have fallen well short of the standard required to resume membership of the ABPI. Unless substantial progress was seen in the report of the re-audits in April 2018, in the Appeal Board's view, Astellas UK would be at serious risk of a recommendation that it be expelled from membership of the ABPI.

**ABPI BOARD FURTHER CONSIDERATION**

The ABPI Board noted the Appeal Board's comments and concerns about the re-audits in October 2017 and the additional information provided by Astellas.

With regard to the external assessment of progress, particularly in relation to risk management of compliance in the broadest sense ie including matters beyond the scope of the Code, the ABPI Board noted the information provided by Astellas. Following a change in tone from the top of Astellas, the ABPI Board recognised that meaningful progress had been made by the companies. The ABPI Board understood the difficulty inherent in making wide-sweeping cultural changes, and how long it took for those changes to become fully embedded within a large organisation. However, the ABPI Board acknowledged Astellas' clear commitment to further improvement.

The ABPI Board noted Astellas' statement that its materials were compliant in May 2017 in relation to issues of patient safety.

The ABPI Board also decided that it wanted sight of the report of the April 2018 re-audits of Astellas UK and Astellas Europe so that it could review the position before the end of the current suspension in June 2018.

The ABPI Board decided that taking all the circumstances into account it would take no further action at this stage in relation to the expulsion of Astellas from membership of the ABPI. The suspension from membership of the ABPI would remain in place until June 2018.

The ABPI Board also decided that the MHRA should be advised of the position. EFPIA should also be updated and asked to ensure that the EFPIA Board was informed of the position.

**APPEAL BOARD FURTHER CONSIDERATION**

In response to a request from the Appeal Board Astellas provided further information which showed that matters raised by the Appeal Board in November were being addressed more promptly than previously indicated.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in April 2018 and the report of the re-audits was considered in May 2018.

The Appeal Board noted the detailed responses from Astellas to the report of the April 2018 re-audits including that it was an accurate reflection of the work undertaken.

The Appeal Board noted the results of the 2018 staff survey and the progress made. Numerical increases had been shown in a number of parameters since the previous survey in July 2017. There were concerns about the comments made by staff. The Appeal Board also noted the differences in the Astellas UK results which were generally better than the Astellas Europe results. The Appeal Board considered that the Astellas Europe management committee scores although improved were still not where they should be.

The Appeal Board noted the comments in the report of the April 2018 re-audits and considered that both the leadership of Astellas Europe and Astellas UK had engaged with staff to bring about progress. There was still work to be done. The Appeal Board noted one of the recommendations was that members of the leadership team at Astellas Europe should be held to account and be challenged on compliance matters.

The Appeal Board accepted that it took time to change a company's culture. In this regard, the Appeal Board noted that there had been further positive changes in the company culture and this needed to be continued. The Appeal Board noted that there had been some positive compliance initiatives. The discussion fora and communications continued and progress had been made including ensuring staff had time to complete training.

The Appeal Board noted that whilst as a percentage there had been a significant increase the number of job bags, the overall numbers was still low. As Astellas increased its activities it must remain extremely vigilant to compliance requirements in particular in relation to certain higher risk activities such as patient support programmes, product launches etc. The true test of the compliance framework in Astellas and its approach would be when activity levels including higher risk activities were increased and the company was operating at business as usual.

The Appeal Board considered that, at long last, the re-audits in April 2018 showed that progress had been made and that the companies were building on momentum started in summer 2017.

The Appeal Board was concerned that these were the fifth audits of each company and that the first audits were in December 2015. It was extraordinary that it had taken so long to demonstrate meaningful change. The overall impression from the report of the April 2018 re-audits was that Astellas was showing improvement and momentum. However, whilst the companies had reached a certain level, given all the circumstances including that Astellas UK had been suspended from membership of the ABPI and that the Appeal Board still had concerns, the Appeal Board decided that Astellas Europe and Astellas UK should each be re-audited at the end of the first quarter of 2019 to ensure that the improvements and the momentum continued and were built upon.

On the information before it, and noting that Astellas UK was still to respond to the PMCPA in relation to matters raised following completion of the consideration of a complaint concerning Astellas UK, Case AUTH/2984/10/17, the Appeal Board decided that sufficient progress had been made by the companies such that the Appeal Board did not consider that it warranted a recommendation for the expulsion of Astellas UK from membership of the ABPI when the matter came before the ABPI Board on 5 June 2018.

**ABPI BOARD FUTHER CONSIDERATION**

In June 2018 the ABPI Board noted the comments from both the Appeal Board and Astellas.

The ABPI Board noted the limited information provided about matters raised in Case AUTH/2984/10/17. This was still to be considered by the PMCPA and the Appeal Board and was not before the ABPI Board for consideration.

The view of the Appeal Board was clear. The ABPI Board agreed with the Appeal Board's views and assessment of the re-audits and concluded that meaningful progress had now been made.

The ABPI Board believed that the culture in the companies had improved and noted that much of this had been led by the General Manager of Astellas UK.

However, the Board recognised the importance of an ongoing commitment to ensure sustained culture change. On reviewing all the material, the ABPI Board had concerns about the sustainability of the changes made given that there had already been five audits/re-audits, and especially as further types of activity were still to be fully re-introduced across the companies.

The ABPI Board therefore decided that it wanted to see the report of the 2019 re-audits and be informed of major developments including the outcome of Case AUTH/2984/10/17.

In the circumstances, there was no need for the ABPI Board to consider expelling Astellas UK from membership of the ABPI. The suspension would end on 24 June 2018 and Astellas would revert to full membership of the ABPI.

Astellas should be cognisant of this ongoing sustainability requirement and monitoring (particularly in light of the matters still to be concluded in Case AUTH/2984/10/17) when communicating about the Board's decision.

The ABPI Board also decided that the MHRA should be advised of the position and that EFPIA should be updated and asked to ensure that the EFPIA Board was informed of the position.

**APPEAL BOARD FURTHER CONSIDERATION**

Astellas UK and Astellas Europe were re-audited in April 2019 and the report of the re-audits was considered in May 2019.

The Appeal Board noted the detailed response from Astellas Europe and Astellas UK to the report of the April 2019 re-audits.

The Appeal Board noted two new senior appointments; a new President EMEA Operations who joined Astellas in July 2018 and a new General Manager, Astellas UK who was appointed from April 2019.

The Appeal Board noted from the report of the April 2019 re-audits that it appeared that a more compliant culture was embedded within Astellas with improved communication. It was essential that this was maintained.

The Appeal Board considered that Astellas UK must ensure a proper professional approach to investigating and responding to any complaint under the Code such that the shortcomings in Case AUTH/2984/10/17 were not repeated. The Appeal Board noted that an audit had not been required in Case AUTH/2984/10/17. The case had, in accordance with established practice, been discussed as part of an examination of the company's culture at the re-audits.

The Appeal Board noted that these were the sixth audits/re-audits of each company and that the first audits were in December 2015. The Appeal Board considered that, on the information provided in the report of the April 2019 re-audits, it appeared that the companies had made further improvements, that this would be maintained and broadly the companies were where they should be. The Appeal Board, however, remained very concerned about the amount of time it had taken Astellas to reach this point. The Appeal Board noted that Astellas stated that it would follow up on the issues identified in the report of the April 2019 re-audits and it was committed to maintaining its approach to embedding a sustainable compliance culture. The Appeal Board noted a number of activities/actions were due to be undertaken. On the understanding that this work was completed, that the progress shown to date was continued and a company-wide commitment to compliance was maintained, the Appeal Board decided that, on the basis of the information in the report of April 2019 re-audits, no further action was required in relation to Case AUTH/2780/7/15, Case AUTH/2883/10/16, Cases AUTH/2939/2/17 and AUTH/2940/2/17.

The Appeal Board noted that the audit/re-audits in these four cases had been required by the Appeal Board. They had not been required by the ABPI Board. Nonetheless, the Appeal Board noted the ABPI Board's request to see the report of the April 2019 re-audits.

At the re-audits in April 2019 it was noted that the MHRA decided that Astellas advertising materials should be submitted for review. This was introduced for all new materials issued since 1 December 2018.

**ABPI BOARD UPDATE**

In June 2019 the ABPI Board received an update as requested. It noted the comments from both the Appeal Board and Astellas and the improvements made.

| | |
|---|---|
| **Voluntary Admission received** | **22 February 2017** |
| **Undertaking received** | **25 April 2017** |
| **Appeal Board Consideration** | **25 May 2017, 16 November, 7 December, 17 May 2018, 22 May 2019** |
| **ABPI Board Consideration** | **6 June 2017, 5 December, 5 June 2018** |
| **ABPI Board update** | **4 June 2019** |
| **Interim case report first published** | **23 June 2017** |
| **Case completed** | **22 May 2019** |

**CASE AUTH/2979/9/17**

# HEALTH PROFESSIONAL v PHARMAMAR

## Certification and Promotion of Yondelis

**An anonymous, non-contactable complainant who described him/herself as a health professional complained about a 'Meetings Highlights' document with the disclaimer 'This newsletter has been funded by an unrestricted educational grant provided by PharmaMar S.A. PharmaMar S.A has not been involved in the production, review or distribution of this material'. The document was on the website of the British Sarcoma Group (BSG). The complainant alleged that PharmaMar had been involved in the preparation of the material which referred to the off-label, early use of its medicine Yondelis (trabectedin).**

**The complainant also listed a number of promotional materials which he/she had been informed had not been certified. The complainant alleged that one piece of material unfairly compared Yondelis with a competitor and another contained unsubstantiated claims.**

**The detailed response from PharmaMar is given below.**

**With regard to the Meetings Highlights document, the Panel noted that it was possible for a company to sponsor material, produced by a third party, which mentioned its own products, and not be liable under the Code for its contents, but only if, *inter alia*, there had been a strictly arm's length arrangement between the parties. In practical terms the arrangements must be such that there could be no possibility that the pharmaceutical company had been able to exert any influence or control over the final content of the material.**

**The Panel considered that the initial arrangements for the production of the Meetings Highlights document were such that PharmaMar was responsible for the content. There was no arm's length arrangement. The Panel did not change its view based on the amendments to the arrangements such that PharmaMar gave the money to BSG so that it could deal with the medical writer etc after the document had been drafted and the company realised the difficulties with the references in the document to the unlicensed use of Yondelis. The Panel also noted that the Meeting Highlights document had been used by the company for a promotional purpose.**

**The Panel considered that the Meeting Highlights document was the responsibility of PharmaMar and as it promoted a medicine for an unlicensed use, the Panel ruled a breach of the Code as acknowledged by the company. The disguised promotional nature of the document was compounded by the inclusion of the disclaimer noted above which was not an accurate description of the company's role. The Panel ruled a breach of the Code as acknowledged by PharmaMar.**

**The Panel ruled that high standards had not been maintained in breach of the Code as acknowledged by the company. The Panel considered that the circumstances brought discredit upon, and reduced confidence in, the pharmaceutical industry and a breach of Clause 2 was ruled as acknowledged by the company.**

**The Panel was extremely concerned that the circumstances showed a very poor understanding of the Code. It was also concerned that an email from a senior executive provided by the complainant showed a disregard for the Code. The Panel noted, however, that this email could not be located on the company's server. PharmaMar submitted that thus its origin and authenticity were not clear. The senior executive in question denied sending the email at issue.**

**The Panel upheld the allegations of an unfair comparison of Yondelis vs a competitor and of unsubstantiated claims. Breaches of the Code were ruled.**

**The Panel was concerned about PharmaMar's arrangements for certification. There was no standard operating procedure and no records of the certificates for the items listed by the complainant. The company could not demonstrate their date of first use or that the materials had been certified. The Panel therefore ruled a breach of the Code as acknowledged by the company.**

**The Panel considered that high standards had not been maintained and that the circumstances brought discredit upon, and reduced confidence in, the pharmaceutical industry. Breaches of the Code were ruled including Clause 2.**

**The Panel was extremely concerned about the conduct of senior employees and the lack of procedures for certification which it considered warranted consideration by the Code of Practice Appeal Board. The Panel therefore decided, in accordance with Paragraph 8.2 of the Constitution and Procedure, to report PharmaMar to the Appeal Board.**

**The Panel also decided that in accordance with Paragraph 7.1 of the Constitution and Procedure PharmaMar should suspend use of the Meeting Highlights document pending the final outcome of the case.**

**The Appeal Board considered that this case raised serious concerns about PharmaMar's processes and Code knowledge. The Appeal Board queried how such a fundamental failure of compliance on what should be well understood principles of the Code could occur. The Appeal Board considered that PharmaMar's investigation into this issue was wholly inadequate. The Appeal Board noted that**

**in response to questioning, PharmaMar stated that its investigation into this case had comprised an IT investigation run by human resources, which found no record of two of the emails provided by the complainant. PharmaMar had provided no documentary evidence to verify its IT investigations.**

**The Appeal Board noted that the PharmaMar representatives submitted that the company had taken advice on this issue from its external review agency yet it provided no documentary evidence to support this.**

**It was wholly unclear why the HR investigation had focussed on the narrow point about the veracity of the two emails rather than giving any consideration to the broader and significant compliance issues pertaining to the newsletter. It was inexplicable that those matters had not been addressed and the Appeal Board queried whether the company truly understood the gravity of the situation including the importance of self-regulation.**

**The Appeal Board noted that the company had provided no record that the member of staff had provided the advice that the company stated it had subsequently followed and that had led to the failings and breaches of the Code. The Appeal Board noted that in response to questioning PharmaMar stated that the member of staff to whom responsibility for the Code was delegated was not a registered signatory. When asked what Code training the company had given the answers were unsatisfactory and vague.**

**The Appeal Board noted that it appeared that the review process was not carried out correctly. The Appeal Board noted that the company's external agency had provided external medical review and in that regard the Code only required one signatory. The company's online approval system did not keep a record of medical certification. PharmaMar had acknowledged that it had failed to certify promotional items. The Appeal Board noted the company's submission that all materials were withdrawn and subject to recertification. The Appeal Board considered that it was shocking that PharmaMar had chosen to delegate responsibility for compliance with the Code without confirming the credentials and knowledge of the individual concerned. The Appeal Board was concerned with the company's lack of process around certification. The Appeal Board considered that the certification process, correctly implemented, underpinned self-regulation. It appeared that there were serious issues regarding PharmaMar's arrangements. The Appeal Board considered that the level of Code expertise within the company appeared to be very poor given the fundamental errors and the company's apparent lack of preparation for the report.**

**The Appeal Board noted the circumstances that gave rise to this case and the company's poor approach to compliance as set out in the Panel's ruling. The Appeal Board noted that PharmaMar had now commissioned a gap analysis to identify, and thereafter start to address, compliance failings. The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, PharmaMar should be publicly reprimanded for failing to make any meaningful effort to undertake a thorough investigation and to provide evidence to support its position. There were significant omissions in its documentation and the company was unable to provide adequate responses to the Appeal Board questions. Such an approach raised grave concerns about the importance attached to compliance and self-regulation by the company. The Appeal Board also decided to require an audit of PharmaMar's procedures in relation to the Code. The audit would take place as early as practicable in early 2018 and on receipt of the report, the Appeal Board would consider whether further sanctions were necessary.**

**The Appeal Board also decided to require PharmaMar to issue a corrective statement to all attendees to the BSG conference and its organisers. [The corrective statement, which was agreed by the Appeal Board prior to use, appears at the end of this report].**

**On receipt of the report for the February 2018 audit the Appeal Board noted the poor internal communication at PharmaMar UK and with its Spanish head office. The Appeal Board considered that PharmaMar in the UK had a very limited compliance structure, compliance expertise and Code knowledge. Leadership on compliance needed to urgently improve. The company lacked many of the basic systems that a company required. It was essential that all staff took an active role in compliance.**

**The Appeal Board noted that the report of the audit highlighted many issues and concerns to be addressed including certification, attention to detail, updating and introduction of standard operating procedures (SOPs) and training. Significant and sustained commitment by all staff was required to address these issues. On receipt of further information in May and June 2018 the Appeal Board decided that PharmaMar should be re-audited in October 2018. On receipt of the report for the re-audit the Appeal Board would decide whether further sanctions were necessary.**

**PharmaMar Spain notified the PMCPA that as of 1 July 2018 the promotional and commercial activities of PharmaMar UK would stop. PharmaMar stated it would leave membership of the ABPI but remain a member of EFPIA.**

**On receipt of this further information at its meeting in July 2018 the Appeal Board noted that as a member of EFPIA, PharmaMar would need to comply with the ABPI Code. The Appeal Board requested further information.**

**On receipt of further information in September 2018 the Appeal Board considered that the PMCPA should make arrangements to re-audit PharmaMar's policies and procedures for how it was running its arrangements in the UK to ensure that PharmaMar was fulfilling its responsibilities under the ABPI Code. The Appeal Board considered that the re-audit should still go ahead as soon as was practical.**

**In October 2018 the Appeal Board noted PharmaMar's response with regard to the Appeal Board's decision that the re-audit of PharmaMar planned for October 2018 should still go ahead at a suitable date in November. The position had changed again. PharmaMar noted that it had now entered into an agreement with Impilo Pharma AB (Medical Need Europe) appointing it as exclusive distributors of Yondelis in a number of territories. The agreement became effective for the UK, on 1 September 2018. The agreement included promotional and medical affairs activities in the UK.**

**The Appeal Board considered that as PharmaMar still held an interest in that it remained the licence holder for Yondelis the re-audit should still go ahead. The re-audit needed to assess how PharmaMar was administering its arrangement with Impilo as to how Yondelis was being marketed in the UK in accordance with the Code. The Appeal Board considered that the re-audit should go ahead as soon as was practical. The Appeal Board noted that the PMCPA would need to see relevant Impilo staff as part of the re-audit.**

**On receipt of the report for the January 2019 re-audit of PharmaMar and Immedica (previously Impilo) in April 2019 PharmaMar SA stated that if and when commercial or medical involvement of UK health professionals was needed, such as speaking at international congresses PharmaMar SA would contact Immedica.**

**In its comments Immedica UK addressed each of the recommendations.**

**The Appeal Board noted from the report of the re-audits that most of the PharmaMar SA staff interviewed considered that the first audit had led to global improvements in culture and processes and they viewed the audit process as an opportunity to improve and change. Staff appeared to show an increased understanding of the importance of compliance.**

**The Appeal Board noted from the report of the re-audits that Impilo Pharma AB as Medical Need and now Immedica, acquired from PharmaMar SA the rights to market and distribute Yondelis in a number of territories including the UK. Immedica UK was a very new small UK company. The Appeal Board noted that the circumstances were unusual in that Immedica UK had not been ruled in breach of the Code. Those interviewed at Immedica UK acknowledged the importance of compliance and the need to ensure that Immedica UK established a robust compliance infrastructure.**

**The Appeal Board noted from the report of the re-audits that it appeared from those interviewed that PharmaMar understood that any future relationships with UK health professionals would be via Immedica headquarters in Sweden and Immedica UK. The Appeal Board considered each company separately. It considered that each company should implement the re-audit reports recommendations.**

**On receipt of further information regarding implementation of recommendations in September 2019 the Appeal Board decided that no further action was required.**

An anonymous, non-contactable complainant who described him/herself as a health professional complained about meeting highlights, sponsored by PharmaMar S.A, from the 13th annual conference of the British Sarcoma Group (BSG). The complainant also alleged that several marketing and sales materials for Yondelis (trabectedin) had not been approved.

Yondelis was indicated, *inter alia*, for the treatment of adults with advanced soft tissue sarcoma after failure of anthracyclines and ifosfamide or who were unsuited to receive these agents.

**COMPLAINT**

The complainant noted that the Meeting Highlights document at issue, available on the BSG website, had the following disclaimer 'This newsletter has been funded by an unrestricted educational grant provided by PharmaMar S.A. PharmaMar S.A. has not been involved in the production, review or distribution of this material'.

The complainant stated, however, that it had been brought to his/her attention that PharmaMar Ltd (UK) had been intrinsically involved in the preparation and content of the material. The material mentioned off-label use of Yondelis. On page 2 under the heading 'Neoadjuvant Chemotherapy' the use of Yondelis was discussed despite it not being licensed for such use. The complainant alleged that this was an attempt to promote off-label early use of the medicine.

The complainant stated that a third-party agency had been involved in the development of the document along with PharmaMar employees as shown by email correspondence provided. In particular, the complainant drew attention to the last message of a senior executive about the BSG newsletter; dated 9 March 2017, it stated 'It is compliant as long as the PMCPA and Madrid are not aware of it'.

The complainant added that he/she had been informed that the following marketing and sales materials produced and distributed by PharmaMar had not been signed off by a medical signatory to avoid compliance review:

- i-pad app screenshots – YON1215-924 – unfair comparison against competitor 'Gem/Tax'
- Exhibition panel – YON0117-1069 – unsubstantiated claims
- Exhibition Advert – YON01170-1070
- Dosing Guide – YON1215-925
- BSG Folder – YON0417-1108
- Treatment Administration Booklet – YON3016-958
- Yondelis Patient Information – YON0816-1009
- Yondelis 6+1 booklet – YON0916-1020.

When writing to PharmaMar the Authority asked it to consider the requirements of Clauses 2, 3.2, 9.1 and 12.1 in relation to the Meeting Highlights document and 2, 9.1, 7.2, 7.4 and 14.1 in relation to the materials.

**RESPONSE**

**a) Meeting Highlights document**

PharmaMar stated that in November 2016 it asked the BSG co-ordinator if there was a potential opportunity to promote Yondelis given that the independently-organised BSG symposium would discuss this medicine. PharmaMar suggested a medical writing agency attend and write a promotional newsletter. The medical writer was well known to the company and had previously written promotional and non-promotional materials for Yondelis. The medical writer was briefed and provided a fee estimate.

The BSG agreed and accordingly two PharmaMar employees and the medical writer attended the symposium (1/2 March 2017) to listen to the content and prepare the promotional newsletter. Some of the symposium content related to the unlicensed use of Yondelis.

On 7 March, the medical writer emailed PharmaMar with suggested content for the newsletter asking for approval and PharmaMar replied that same day with suggestions. It was extremely unfortunate that the reference in the medical writer's email to the unlicensed use of Yondelis (neo-adjuvant chemotherapy for soft tissue sarcoma) was not picked up by the two PharmaMar employees involved or during the symposium itself.

However, the following day (8 March) email correspondence between the two employees who had attended the symposium noted that the suggested content for the newsletter contained information in relation to the unlicensed use of Yondelis, that a promotional newsletter could not include this and that the newsletter would also require prescribing information. The medical writer was not copied in.

PharmaMar submitted that at this point, the promotional newsletter could have simply omitted the unlicensed information but the topic of neo-adjuvant chemotherapy for soft tissue sarcoma was a key highlight of the meeting and could not therefore be left out of a Meeting Highlights newsletter.

It would appear that on advice from one company attendee, the more senior company attendee (a senior executive) contacted the BSG co-ordinator to alert him/her that the newsletter could no longer be promotional, should now be supported by a grant and that the company should have no further involvement. The BSG acknowledged this point and requested disclaimer wording, which was subsequently provided by the less senior company attendee.

On the basis of the senior executive's email, the medical writer would write a comprehensive meeting report (reflecting the content of the symposium and thus containing both licensed and unlicensed information about Yondelis) and the BSG Board would fund and approve this, with no involvement of PharmaMar other than financial support via a grant to the BSG. Therefore, PharmaMar did not review the newsletter.

(PharmaMar provided a copy of the medical writer's invoice to the BSG).

PharmaMar fully acknowledged that it was not possible to establish an arm's length arrangement with the newsletter for the following reasons, and it was thus responsible for its content:

1 The engagement of a medical writer to develop a symposium newsletter was initiated by PharmaMar.
2 Company staff knew the newsletter would in effect promote Yondelis for an unlicensed indication.

Once certain staff understood the full content of the newsletter, they naïvely suggested that it could be supported by a grant from PharmaMar in order to allow the publication to continue and provided a declaration of sponsorship in that regard. This demonstrated a poor understanding of the requirements of the Code by those involved.

PharmaMar stated that it did not deliberately intend to breach the Code but accepted that the content of a publication for which it was responsible promoted one of its medicines for an unlicensed indication, and was disguised in that regard. With this in mind, PharmaMar acknowledged breaches of Clauses 3.2, 12.1, 9.1 and 2 and apologised unreservedly.

PharmaMar stated that it was unfortunate that its senior executive appeared to have acted in good faith but was badly advised on this approach by a less senior colleague and that no-one involved with the publication (including the experienced medical writer) recognised the inappropriate nature of the activity, despite their senior positions and industry experience.

PharmaMar stated that the email in which it was stated 'It is compliant as long as the PMCPA and Madrid are not aware of it', provided by the complainant, could not be located on any of its servers and thus its origin and authenticity was not clear. The attributed author categorically denied that he/she had ever stated, either verbally or in writing, that the report was 'compliant as long as the PMCPA and Madrid are not aware of it'.

**b) Review and Certification**

In order to describe the process of review and approval of promotional and non-promotional materials, PharmaMar provided some background and important dates including:

- September 2015: PharmaMar Ltd UK affiliate was formally established and the two employees at issue (and others) were transferred to PharmaMar Ltd UK. A third party was retained to provide external medical review of material
- April 2016: The company joined the ABPI
- August 2016: New UK Country Manager appointed
- September 2016: The contract with the external review agency was extended to include certification as well as review support.

PharmaMar provided a copy of its current Global standard operating procedure (SOP) on 'Drafting and approval of promotional materials for the EU and

Switzerland' which stated that the approval process might involve several different reviewers (Spain marketing, Spain regulatory, UK marketing and UK medical). The online approval system, CLEARANCE, stored a record of the PharmaMar UK approval of each item but not the comments made by the external review agency or the medical certification of each. Storage of the agency's comments and approval relied solely on emails between it and PharmaMar (specifically the two employees at issue).

PharmaMar submitted it was highly regrettable that an equivalent UK SOP on the approval of promotional and non-promotional activities and materials was not in place – it was being developed as a matter of urgency with implementation anticipated no later than 31 October. PharmaMar thus had no record of the requisite certificates having been signed to verify signatory confirmation of compliance with the Code for any of the items referred to by the complainant, nor did it have a record of the date of first use of each item.

PharmaMar acknowledged that it had failed to certify promotional items, in breach of Clause 14.1 due to failings in its certification process. It also acknowledged that this amounted to a failure to maintain high standards, in breach of Clause 9.1.

With respect to the allegation of 'unfair comparison vs Gem/Tax' (gemcitabine/docetaxel) in the ipad app (ref YON1215-924), the table in the ipad app compared various attributes such as recommendations from the National Institute for Health and Care Excellence (NICE) and European Society for Medical Oncology (ESMO) – this information was intended to be accurate but on further scrutiny of the guidelines, the information in the app was incomplete and therefore did not fully represent the evidence. Therefore PharmaMar accepted the comparison was unfair and in breach of Clause 7.2 in this regard.

With respect to the allegation that the claim 'Gem/Tax – Higher toxicity' on stand material could not be substantiated, although this information appeared to be from head-to-head data, this was not actually the case and therefore the misleading impression could not be substantiated. PharmaMar accepted a breach of Clause 7.4.

PharmaMar acknowledged that the lack of a robust process in relation to certification, which was essential for self-regulation, amounted to a breach of Clause 2 and it gave its assurance that it was addressing this failing as a matter of urgency.

**Summary**

In summary, PharmaMar stated that it took very seriously its commitment to adhere to the Code and appreciated that self-regulation was a privilege. In that vein, it would be immediately implementing corrective and preventative actions to avoid future breaches of the Code. This would include, *inter alia*, the following:

- PharmaMar Ltd UK would hire a head of medical affairs to act as final medical signatory. This individual would also have compliance responsibilities and oversight.
- UK-specific SOPs would be created to cover all activities and materials under the scope of the UK Code. These would be trained out to UK staff and implemented effectively.
- Code training had taken place in the past but PharmaMar would provide refresher training to all relevant staff on the requirements of the Code.
- Relationships with third party agencies would be reviewed to ensure due diligence at the outset, that they were trained and had sufficient experience and knowledge of the Code to continue to provide support.
- Certification systems and processes would be overhauled so that Clause 14 requirements around signatories, certificates and archival were met.
- Further action with employees would be considered if the above activities were insufficient.

**PANEL RULING**

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure stated that anonymous complaints would be accepted, but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant could not be contacted for further information.

With regard to the Meetings Highlights document, the Panel noted that it was possible for a company to sponsor material, produced by a third party, which mentioned its own products, and not be liable under the Code for its contents, but only if, *inter alia*, there had been a strictly arm's length arrangement between the parties. In practical terms the arrangements must be such that there could be no possibility that the pharmaceutical company had been able to exert any influence or control over the final content of the material. Factors which might mean there had not been a strictly arm's length arrangement would include, but not be restricted to:

- Initiation of the material, or the concept for it, by the pharmaceutical company
- Influence from the pharmaceutical company on the content/balance/scope of the material
- Choice/or direct payment of the authors by the pharmaceutical company
- Influence from the pharmaceutical company on the list of persons to whom the material was sent.

The Panel noted the initial arrangements for the Meetings Highlights document. It did not considered that PharmaMar had sponsored that content. The company's initial involvement in making all the arrangements for production of the Meetings Highlight document was such that in the Panel's view the company was responsible for the content. It was not an arm's length arrangement. The Panel did not change its view based on the amendments to the arrangements made by the company such that PharmaMar gave the money to BSG so that it could deal with the medical writer etc after the document had been drafted and the company realised the difficulties with the references in the document to the unlicensed use of Yondelis.

The Meeting Highlights document had been used by the company for a promotional purpose.

The Panel considered that the Meeting Highlights document was the responsibility of PharmaMar and as it promoted a medicine for an unlicensed use, the Panel ruled a breach of Clause 3.2 of the Code as acknowledged by the company. The document was disguised promotion. The disguised nature was compounded by the inclusion of the disclaimer that 'This newsletter had been funded by an unrestricted educational grant provided by PharmaMar S.A. PharmaMar S.A. had not been involved in the production review or distribution of this material' which was not an accurate description of the role of the company. The Panel ruled a breach of Clause 12.1 of the Code as acknowledged by the company.

The Panel ruled that high standards had not been maintained in breach of Clause 9.1 of the Code as acknowledged by the company. Clause 2 was a sign of particular censure and was reserved for such use. The Panel considered that the circumstances brought discredit upon, and reduced confidence in, the pharmaceutical industry and a breach of Clause 2 was ruled as acknowledged by the company.

The Panel was extremely concerned that the changes to the Meeting Highlights document suggested by PharmaMar showed a very poor understanding of the Code. It was also concerned that the email, allegedly from a senior executive, showed a disregard for the Code. The Panel noted, however that the email could not be located on the company's server. PharmaMar submitted that thus its origin and authenticity were not clear. The employee categorically denied stating that '… it is compliant as long as the PMCPA and Madrid are not aware of it'.

The Panel noted that with regard to the ipad screenshots and the reference to the unfair comparison of 'Gem/Tax' (gemcitabine and docetaxel) and Yondelis, PharmaMar acknowledged that the information about NICE and ESMO was incomplete. The Panel therefore ruled a breach of Clause 7.2 in relation to the acknowledged misleading comparison.

The Panel also ruled a breach of Clause 7.4 with regard to a failure to substantiate a claim that Gem/Tax had a higher toxicity noting PharmaMar's submission that the data appeared to be from a head-to-head study and this was not so.

The Panel was concerned about PharmaMar's arrangements for certification. There was no SOP and there were no records of the certificates for the items listed by the complainant. The company could not demonstrate their date of first use or that the materials had been certified. The Panel therefore ruled a breach of Clause 14.1 in relation to the promotional items as acknowledged by the company. The Panel noted that the case preparation manager had not cited any other sub-clause in relation to these allegations. There was no certification record for patient materials as required by Clause 14.2 and Clause 14.6 set out the requirements for preserving certificates and other documentation.

The Panel considered that high standards had not been maintained with regard to the arrangements for certification at PharmaMar and it thus ruled a breach of Clause 9.1 of the Code as acknowledged by the company. The Panel considered that the circumstances brought discredit upon, and reduced confidence in, the pharmaceutical industry and therefore ruled a breach of Clause 2 of the Code.

The Panel was extremely concerned about the conduct of senior employees and the lack of procedures for certification which it considered warranted consideration by the Code of Practice Appeal Board. The Panel therefore decided, in accordance with Paragraph 8.2 of the Constitution and Procedure, to report PharmaMar to the Appeal Board.

The Panel also decided that in accordance with Paragraph 7.1 of the Constitution and Procedure PharmaMar should suspend use of the Meeting Highlights document pending the final outcome of the case.

**COMMENTS FROM PHARMAMAR ON THE REPORT FROM THE PANEL**

At the consideration of the report the representatives from PharmaMar stated that the company had accepted the Panel's rulings of breaches of the Code and it sincerely apologised for the failings in this case. The company intended to do whatever was necessary to ensure that this issue was not repeated. In that regard the company had invested in third party Code expertise that had detected gaps in its processes and its priority was to address these issues. The company was also employing the services of a third party signatory and it was in the process of hiring a permanent head of medical affairs. All previous promotional material had been withdrawn and a review process of compliance was ongoing.

**APPEAL BOARD CONSIDERATION OF THE REPORT FROM THE PANEL**

The Appeal Board noted the Panel's comments and rulings above including the ruling of a breach of Clause 2 which PharmaMar had accepted. The Appeal Board also noted that PharmaMar apologised for its failings in this case.

The Appeal Board considered that this case raised serious concerns about PharmaMar's processes and Code knowledge. The Appeal Board queried how such a fundamental failure of compliance on what should be well understood principles of the Code could occur. The Appeal Board considered that PharmaMar's investigation into this issue was wholly inadequate.

The Appeal Board noted that in response to questioning PharmaMar stated that its investigation into this case had comprised an IT investigation run by human resources, which found no record of two of the emails provided by the complainant dated 9 March. These comprised an email to a senior executive that stated '…I have to inform you that

the newsletter as it is will not be compliant'; and the reply that stated 'It is compliant as long as the PMCPA and Madrid are not aware of it'. PharmaMar had provided no documentary evidence to verify its IT investigations. The Appeal Board noted the submission of the company representatives about the veracity of the emails at the hearing which included matters of style, format and the whereabouts of the senior executive on 9 March. The company confirmed that the preceding email sent to the senior executive on 8 March was genuine. The email stated 'From a Code Compliance point of view this will be considered promotional as it mentions trabectedin. This will mean it will require Prescribing Information and the neo adjuvant part has to be taken out as it is off label'. The sender then asked to be provided with details of the arrangements with two named individuals to see if he could come up with an alternative solution and finished '… call me if you need more clarification'. The Appeal Board considered that contrary to the inferences of the company representatives, this email appeared to give the correct initial advice and yet in response to questioning the PharmaMar representatives stated that that they did not know and had not investigated what response the senior executive had given to this email. At the hearing in response to questioning the senior executive stated that he/she did not know how he/she had responded to the email.

The Appeal Board noted that the PharmaMar representatives submitted that the company had also taken advice on this issue from its external review agency yet again it provided no documentary evidence to support this.

It was wholly unclear why the HR investigation had focussed on the narrow point about the veracity of the two emails rather than giving any consideration to the broader and significant compliance issues pertaining to the newsletter. It was inexplicable that those matters had not been addressed and the Appeal Board queried whether the company truly understood the gravity of the situation including the importance of self-regulation.

The Appeal Board noted that the company had provided no record that the member of staff had provided the advice that the company stated it had subsequently followed and that had led to the failings and breaches of the Code. The Appeal Board noted that in response to questioning PharmaMar stated that the senior executive and his/her predecessor had delegated responsibility under the Code to this staff member and the company had subsequently discovered that this member of staff was not a registered signatory. When asked what Code training the company had given the member of staff the company's answers were unsatisfactory and vague. The Appeal Board noted that it appeared that the review process was not carried out correctly and in this regard it noted the person's credentials. The Appeal Board noted that the company's external agency had provided external medical review and in that regard the Code only required one signatory. The company's online approval system did not keep a record of medical certification. The Appeal Board noted that PharmaMar had acknowledged that it had failed to certify promotional items. The Appeal Board noted the company's submission that all materials were withdrawn and subject to recertification. The Appeal Board considered that it was shocking that PharmaMar had chosen to delegate responsibility for compliance with the Code without confirming the credentials and knowledge of the individual concerned. The Appeal Board was concerned with the company's lack of process around certification. The Appeal Board considered that the certification process, correctly implemented, underpinned self-regulation. It appeared that there were serious issues regarding PharmaMar's arrangements. The Appeal Board considered that the level of Code expertise within the company appeared to be very poor given the fundamental errors and the company's apparent lack of preparation for the report.

The Appeal Board noted the circumstances that gave rise to this case and the company's poor approach to compliance as set out in the Panel's ruling. The Appeal Board noted that PharmaMar had now commissioned a gap analysis to identify, and thereafter start to address, compliance failings.

The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, PharmaMar should be publicly reprimanded for failing to make any meaningful effort to undertake a thorough investigation and to provide evidence to support its position. There were significant omissions in its documentation and the company was unable to provide adequate responses to the Appeal Board questions. Such an approach raised grave concerns about the importance attached to compliance and self-regulation by the company. The Appeal Board also decided to require an audit of PharmaMar's procedures in relation to the Code. The audit would take place as early as practicable in early 2018 and on receipt of the report, the Appeal Board would consider whether further sanctions were necessary.

The Appeal Board also decided to require PharmaMar to issue a corrective statement to all attendees to the BSG conference and its organisers. [The corrective statement, which was agreed by the Appeal Board prior to use, appears at the end of this report].

**APPEAL BOARD FURTHER CONSIDERATION**

On receipt of the report for the February 2018 audit the Appeal Board noted the poor internal communication at PharmaMar UK and with its Spanish head office. The Appeal Board considered that PharmaMar in the UK had a very limited compliance structure, compliance expertise and Code knowledge. Leadership on compliance needed to urgently improve. The company lacked many of the basic systems that a company required. It was essential that all staff took an active role in compliance.

The Appeal Board noted that the report of the audit highlighted many issues and concerns to be addressed including certification, attention to detail, updating and introduction of standard operating procedures (SOPs) and training. Significant and

sustained commitment by all staff was required to address these issues. On receipt of further information in May and June 2018 the Appeal Board decided that PharmaMar should be re-audited in October 2018. On receipt of the report for the re-audit the Appeal Board would decide whether further sanctions were necessary.

**FURTHER CONSIDERATION OF THE APPEAL BOARD**

PharmaMar Spain notified the PMCPA that as of 1 July 2018 the promotional and commercial activities of PharmaMar UK would stop. PharmaMar stated it would leave membership of the ABPI but remain a member of EFPIA.

On receipt of this further information at its meeting in July 2018 the Appeal Board noted that as a member of EFPIA, PharmaMar would need to comply with the ABPI Code. The Appeal Board requested further information.

On receipt of further information in September 2018 the Appeal Board considered that the PMCPA should make arrangements to re-audit PharmaMar's policies and procedures for how it was running its arrangements in the UK to ensure that PharmaMar was fulfilling its responsibilities under the ABPI Code. The Appeal Board considered that the re-audit should still go ahead as soon as was practical.

On receipt of further information in October 2018 the Appeal Board noted PharmaMar's response with regard to the Appeal Board's decision that the re-audit of PharmaMar planned for October 2018 should still go ahead at a suitable date in November despite the closing down of Pharma Mar Ltd operations in the UK as of 31 July 2018 and its UK office as of 30 August 2018. The position had changed again. PharmaMar noted that it had now entered into an agreement with Impilo Pharma AB (Medical Need Europe) appointing it as exclusive distributors of Yondelis in a number of territories. The agreement became effective for the UK, on 1 September 2018. The agreement included promotional and medical affairs activities in the UK.

The Appeal Board considered that as PharmaMar still held an interest in that it remained the licence holder for Yondelis the re-audit should still go ahead. The re-audit needed to assess how PharmaMar was administering its arrangement with Impilo as to how Yondelis was being marketed in the UK in accordance with the Code. The Appeal Board considered that the re-audit should go ahead as soon as was practical. The Appeal Board noted that the PMCPA would need to see relevant Impilo staff as part of the re-audit.

On receipt of the report for the January 2019 re-audit of PharmaMar and Immedica (previously Impilo) in April 2019 PharmaMar SA stated that if and when commercial or medical involvement of UK health professionals was needed, such as speaking at international congresses PharmaMar SA would contact Immedica.

In its comments Immedica UK addressed each of the recommendations.

The Appeal Board noted from the report of the re-audits that most of the PharmaMar SA staff interviewed considered that the first audit had led to global improvements in culture and processes and they viewed the audit process as an opportunity to improve and change. Staff appeared to show an increased understanding of the importance of compliance.

The Appeal Board noted from the report of the re-audits that Impilo Pharma AB as Medical Need and now Immedica, acquired from PharmaMar SA the rights to market and distribute Yondelis in a number of territories including the UK. Immedica UK was a very new small UK company. The Appeal Board noted that the circumstances were unusual in that Immedica UK had not been ruled in breach of the Code. Those interviewed at Immedica UK acknowledged the importance of compliance and the need to ensure that Immedica UK established a robust compliance infrastructure.

The Appeal Board noted from the report of the re-audits that it appeared from those interviewed that PharmaMar understood that any future relationships with UK health professionals would be via Immedica headquarters in Sweden and Immedica UK. The Appeal Board considered each company separately. It considered that each company should implement the re-audit reports recommendations.

On receipt of further information regarding implementation of recommendations in September 2019 the Appeal Board decided that no further action was required.

| | |
|---|---|
| **Complaint received** | **21 September 2017** |
| **Undertaking received** | **27 November 2017** |
| **Appeal Board consideration** | **7 December 2017, 18 April, 17 May and 20 June, 19 July, 13 September, 17 October 2018, 10 April, 18 September 2019** |
| **Interim case report first published** | **9 April 2018** |
| **Case completed** | **18 September 2019** |

On 9 April 2018, BSG sent the following corrective statement on behalf of PharmaMar to all attendees to the BSG conference and its organisers.

> 'Corrective statement
>
> Between March and October 2017, the 'British Sarcoma Group 13th Annual Conference, 1st - 2nd March 2017 – Meeting Highlights' newsletter was available. The newsletter mentioned Yondelis (trabectedin) which was marketed by PharmaMar Ltd.
>
> You are being sent this corrective statement because you received or might have received the newsletter.
>
> Following a complaint under the ABPI Code of Practice for the Pharmaceutical Industry, the Code of Practice Panel considered that the newsletter was the responsibility of PharmaMar and it promoted its medicine for an unlicensed use. The document was also disguised promotion and the disguised nature was compounded by the inclusion of the disclaimer that 'This newsletter had been funded by an unrestricted educational grant provided by PharmaMar S.A. PharmaMar S.A. had not been involved in the production review or distribution of this material' which was not an accurate description of the role of the company
>
> The Code of Practice Panel ruled that PharmaMar had failed to maintain high standards and had brought discredit upon and reduced confidence in the pharmaceutical industry. As a result of the above governance concerns, the Panel reported PharmaMar to the Code of Practice Appeal Board which required PharmaMar to issue this corrective statement and to circulate a copy of the published report for the case which contains full details. This is enclosed.

Details of this case (Case AUTH/2979/9/17) are also available on the PMCPA website (www.pmcpa.org.uk).'

CASE AUTH/3013/1/18

# ASTRAZENECA EMPLOYEE v ASTRAZENECA

## Global training and advisory board and provision of incomplete and inaccurate information

**An anonymous, non-contactable complainant, who described him/herself as an employee of AstraZeneca UK Limited's marketing company, alleged that although one of AstraZeneca's values was 'we do the right thing', over the last five years the company had become solely focussed on profits ahead of its ethical obligations. Over the last couple of years, the trend had reversed in the UK marketing company and the focus on achieving AstraZeneca's goals through the right means had returned. However, the same was not so for AstraZeneca's global functions.**

**The complainant stated that as a UK company, and with many employees in the global functions based in the UK, AstraZeneca should comply with the Code for activities led by global. However, this was not so. Global functions did not receive appropriate training on the Code and did not have regular Code case updates as in the UK marketing company. Globally led activities thus usually did not comply with the Code. In particular, the complainant referred to an unspecified global advisory board, held in October 2017, with over 15 external advisors and a similar number of AstraZeneca employees. The UK nominated signatory who was asked to approve the meeting, as UK health professionals were advisors, refused to do so due to the excessive number of people and the view that this was not a genuine advisory board. However, the UK marketing company was put under pressure to approve this and the nominated signatory was told to approve the advisory board by two other staff even though they acknowledged that it was likely to be a breach of the Code.**

**The detailed response from AstraZeneca is given below.**

**With regard to the allegations about training, the Panel noted that AstraZeneca distributed training to staff based on their role, location and responsibilities. The Panel noted that although the materials provided by AstraZeneca did not demonstrate comprehensive training on the Code, the company nonetheless trained global staff and provided more detailed training to the nominated signatories. The Panel did not consider that there was evidence to show that on the balance of probabilities, AstraZeneca had not trained relevant global staff as alleged. The Panel therefore ruled no breach of the Code.**

**With regard to advisory boards, the Panel noted that it was acceptable for companies to pay health professionals and others for relevant advice. Nonetheless, the arrangements for such meetings had to comply with the Code. To be considered a legitimate advisory board the choice and number of participants should stand up to independent scrutiny; each should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the advisory board. The number of participants should be limited so as to allow active participation by all. The agenda should allow adequate time for discussion. The number of meetings and the number of participants should be driven by need and not the invitees' willingness to attend. Invitations to participate should state the purpose of the meeting, the expected advisory role and the amount of work to be undertaken. If an honorarium was offered it should be made clear that it was a payment for such work and advice. Honoraria must be reasonable and reflect the fair market value of the time and effort involved.**

**AstraZeneca referred to an advisory board meeting, held in Amsterdam in November 2017, which, in the absence of details, it assumed was the one to which the complainant had referred. The Panel noted that the agenda for that advisory board, included in the presentation, started with a welcome coffee and the actual meeting started at 10.30am and ended at 5.30pm; there were breaks for lunch and tea. The meeting was co-chaired by an external speaker and a member of AstraZeneca staff. One of the two speakers in the morning session was from AstraZeneca and the moderators for the afternoon discussion groups were both from AstraZeneca.**

**The initial invitation described the advisory board as part of AstraZeneca's ongoing commitment to supporting health professionals and patients. The objective of the meeting was to gain expert feedback and insights on the role of selective sodium glucose co-transporter 2 (SGLT2) inhibitors in type 1 diabetes and specifically the Forxiga (dapagliflozin) programme studies (DEPICT-1 and -2). The external speaker was asked to critically evaluate the benefit/risk of dapagliflozin on type 1 diabetics and to provide recommendations for safe and effective use of dapagliflozin in type 1 diabetes.**
**The UK delegates were emailed 6 published papers as pre-reading 6 days before the meeting.**

**There were 78 slides to be used during the day. Twenty-eight slides were presented in the first session by an external speaker, one of the investigators of the DEPICT studies. This one-hour session, which focused on the results of the two studies included two periods for discussion. The second session of seventeen slides, presented by an AstraZeneca employee, focused on the safety results of the two studies and lasted for one hour and fifty minutes. In the afternoon the group was split into**

**two (US and EU/International) and each group, moderated by AstraZeneca, discussed as session 3 (45 mins) the efficacy results. Session 4 (90 minutes) was a discussion of the benefit/risk of dapagliflozin in type 1 diabetes. The day ended with 30 minutes for summary and closing remarks. The short agenda provided included the sub heading 'Group discussion is 80% or more of each allocated session time and includes all participants'.**

**The Panel queried whether so many slides were needed on the DEPICT outcomes given the prereading included the published studies.**

**The Panel noted that the advisory board was to help AstraZeneca decide about an application for a new indication in the US and EU. In that regard, seven of the 16 advisors were from the US, eight came variously from five European countries (two from the UK, a doctor and a diabetes specialist nurse) and one advisor was from another country. In addition, there were 12 AstraZeneca staff.**

**The rationale for the attendance of AstraZeneca staff was provided. The stated business justification was to present and discuss DEPICT data, to critically evaluate benefit/risk of dapagliflozin on type 1 diabetes patients and to provide recommendations for the safe and effective use of dapagliflozin in type 1 diabetes. The business justification in this document was different to the objectives provided to the attendees. This document listed the 12 AstraZeneca staff and the rationale for their attendance. Five of the staff were to watch the first part of the advisory board via a video link and then three would actively participate in the breakout sessions. This was different to the submission from the company which stated that 9 of its staff joined the meeting and three listened in another room. Following a request for further information, the company stated that on the day there were 9 AstraZeneca staff in the room and the three listening in another room joined the main room about half way through the morning session due to a technical problem.**

**From the list of AstraZeneca attendees, four were assigned to participate in each of the breakout sessions; it was not stated if the other four were to participate in either session or not. The further information confirmed that all 12 AstraZeneca staff participated in the afternoon breakout sessions.**

**It was not clear to the Panel why AstraZeneca had not described what actually happened at the advisory board in the first instance. It was unacceptable and concerning that details of the arrangements for AstraZeneca attendees were only provided following a request for additional information.**

**The Panel was concerned about a number of aspects of the advisory board including the number of AstraZeneca attendees which was well outside the UK SOP. However, this did not necessarily mean that the advisory board failed to meet the requirements of the ABPI Code. The Panel was concerned to note, given the compliance difficulties that companies could experience with advisory boards and the high profile given to such in the UK recently, that it appeared that the arrangements for the meeting were only submitted for local review 12 working days before the meeting took place. The Panel was also concerned that the day before the advisory board AstraZeneca made fundamental changes to the arrangements and increased the number of its staff in the meeting room. In the Panel's view, the timescales and last minute changes would put unnecessary pressure on the nominated signatory to approve a meeting for which all of the arrangements should have already been in place; the UK SOP stated that material should be submitted for approval at least 6 weeks before the meeting date.**

**The Panel noted that no evidence was supplied in relation to the alleged pressure on the UK signatory to certify the meeting. The Panel was concerned as this was a serious allegation and it was vital that signatories were free to decline certifying material if they did not think it met the requirements of the Code. It appeared from AstraZeneca's submission that there was discussion between UK and global. This was particularly concerning given that this was ongoing so close to the date of the advisory board and that advisory boards were high risk area for companies. The Panel queried whether the certification should have been completed before the UK advisors were first approached at the end of September. If the arrangements were not capable of certification, UK health professionals should not have been approached.**

**The Panel noted that the advisory board which was held outside the UK and involved UK delegates had not been certified. The Panel noted AstraZeneca's submission that this was due to a timing issue rather than because the signatory was concerned with compliance with the Code. The Panel ruled that the failure to certify was in breach of the Code as acknowledged by AstraZeneca.**

**The Panel noted the complainant alleged that the advisory board was not genuine. No evidence had been provided by the complainant who had not clearly identified the advisory board about which he/she was concerned. As noted above, the Panel was concerned about the advisory board identified by AstraZeneca but did not consider that the complainant had shown, on the balance of probabilities, that the advisory board held on 10 November 2017 failed to meet the requirements of the Code and thus that any payment was inappropriate. Thus, the Panel ruled no breach of the Code.**

**On balance, the Panel considered that the arrangements for certification and the short time frame increased the pressure on UK certifiers. This and the failure to certify meant that AstraZeneca had failed to maintain high standards and a breach was ruled.**

**Noting its rulings above the Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such use.**

**ADDENDUM TO SUMMARY**

**Following completion of this case in April 2018 and its publication on the PMCPA website in May 2018 a letter was received in June 2018 regarding the case and providing further information. It appeared to have come from the original anonymous, non-contactable complainant, who had described him/herself as an employee of AstraZeneca UK Limited.**

**The letter appeared to provide information which had not been provided by AstraZeneca in its response to the complaint: an email from a senior UK medical department employee outlining options for the advisory board in question. The further information was provided to AstraZeneca for comment including on Case AUTH/2793/9/15 where additional information was provided following the completion of a case.**

**Detailed comments from the complainant and AstraZeneca are given below.**

**The PMCPA decided that the original Panel should reconvene to consider the matter in relation to Paragraph 8.2 of the Constitution and Procedure which provided that the Panel might report to the Appeal Board any company whose conduct in relation to the Code, or in relation to a particular case before it, or because it repeatedly breached the Code such that it raised concerns about the company's procedures, warranted consideration by the Appeal Board. Such a report to the Appeal Board might be made notwithstanding the fact that a company had provided an undertaking requested by the Panel. The Panel noted that AstraZeneca had provided the requisite undertaking.**

**The Panel noted that the author of the letter had provided a copy to the Medicines and Healthcare products Regulatory Agency (MHRA) as the author was concerned there appeared to be no activity and alleging that AstraZeneca was receiving preferential treatment. The PMCPA responded to inform the MHRA that the matter had been followed up with AstraZeneca and would be considered by the Panel shortly. The delay was due to the number of complex cases. AstraZeneca was not receiving any preferential treatment.**

**The Panel noted the difficulties for UK companies regarding activities run by global.**

**The Panel noted the email trail dated 7 and 8 November 2017 provided as additional information which appeared to provide context to the discussions between the UK company and the global company about the arrangements for the advisory board held on 10 November 2017. It was clear that the concerns raised by the UK went beyond just a difference between the UK and global SOPs. Reference was made to advisory boards being in the spotlight in the UK over the last 18 months. The MHRA had questioned the validity of advisory boards and that the UK position was rather sensitive at the moment due to the AstraZeneca cases at the Panel and that it was '… trying to ensure we do not attract an audit'. The senior UK medical department employee stated that the need for the global advisory board was clear and the agenda was reasonable. The ratio of AstraZeneca attendees to health professionals was high. The situation was described as low risk but if a complaint were made it would be marginal as to whether it could be defended from a perceptual perspective. Three options were proposed including option 1 that the extra 5 AstraZeneca attendees watched the first part of the advisory board in a separate room and then participated in the breakout sessions. The email trail went on to state that the senior UK medical department employee wanted to avoid dropping the UK health professionals and also disrupting the plans for the proposed agenda. He/she was happy to go with any of the three options. He/she understood that this was frustrating but 'we do need to be consistent in our approach to implementing the code'.**

**The Panel considered that it was not clear from the email trail whether the senior UK medical department employee considered that the number of AstraZeneca attendees at the advisory board was in breach of the Code or in breach of the AstraZeneca UK SOP. The email spelt out three options. The Panel noted that the company had decided on option 1 although as included in the report for Case AUTH/3013/1/18 this did not happen due to technical issues.**

**The Panel considered the email including the context of discussions about the advisory board and the perception of the email. The Panel considered that the reference to self-reporting was a possible reference to the need for AstraZeneca to consider making a voluntary admission about a possible breach of the Code. Clearly it was important that companies followed their SOPs but not doing so was not in itself necessarily a breach of the Code.**

**The impression of the email was that the UK company had concerns about the arrangements for the advisory board, in particular the number of AstraZeneca attendees. Full details about the number of AstraZeneca attendees had only been provided to the Panel considering the case when it asked for further information.**

**The Panel noted that clearly there were difficulties with the advisory board and breaches of the Code had been ruled and a number of concerns raised. At that time it was also clear that AstraZeneca had not provided all the information. In relation to AstraZeneca's submission that as the Panel had not asked for the email of 8 November it had not provided the email, the Panel noted that self-regulation relied on companies to provide all relevant material. As the Panel did not know of the existence of the email, it could not request it.**

**The Panel noted AstraZeneca's submission that the email represented a snapshot of the discussions that had taken place and these were explained in the company's response to Case AUTH/3013/1/18 where it stated 'they presented several options to resolve this, one of which was the option which was eventually settled upon'.**

**Now having received the email of 8 November the Panel did not consider that this additional information would have made a difference as to whether it thought the advisory board itself was in breach of the Code. The Panel had ruled no breach in this regard based on the complainant not having shown on the balance of probabilities that there was a breach of the Code. However, the new information which provided some insight into the company's compliance culture was a concern as was AstraZeneca's general approach with regard to providing information to the Panel as evidenced by the number of times recently that the company had either not provided all the relevant information or had provided misleading information. This was set out in the Panel's request for further information from AstraZeneca.**

**Taken as a whole, the Panel considered that AstraZeneca could not clearly demonstrate its stated commitment to self-regulation in the broadest sense. It was concerned that actions might be taken by AstraZeneca so as to '… not attract an audit' rather than ensuring compliance with the Code and its own procedures. The Panel was also concerned that it appeared from the email and other aspects of the complaint that for some staff raising concerns about activities was difficult at AstraZeneca and this contributed to the differences of opinion between UK and Global. However, it decided that, on balance, the material before it, most of which had come to light either during the consideration of the cases or afterwards and had been the subject of a public reprimand, had been addressed and thus on balance a formal report to the Appeal Board was not needed at this stage. The Panel's view was that these examples should be reconsidered if there were further instances of AstraZeneca failing to provide comprehensive information. The Appeal Board would be provided with details of the Panel's further consideration following a similar format to the details provided for cases which concluded at the Panel level.**

**The Appeal Board received the update to the case report as set out in Paragraph 13.4 of the Constitution and Procedure.**

**The Appeal Board considered that the additional information in this case raised serious issues including about the provision of incomplete and/ or inaccurate information. The Appeal Board's view was that further consideration should be given to this matter including the possibility of imposing further sanctions under Paragraph 11.1 of the Constitution and Procedure.**

**The company was advised that the Appeal Board was giving further consideration to this matter including considering imposing additional sanctions and asked to respond in writing, as well as be given the opportunity to attend the Appeal Board when the matter would be considered. AstraZeneca was provided with a copy of the papers.**

**The detailed comments from AstraZeneca about the possible imposition of further sanctions is given below.**

**The Appeal Board noted the Panel's rulings of breaches of the Code. The Appeal Board noted that the company had apologised and admitted that it had made errors.**

**The Appeal Board noted the context in that there had been discussions between AstraZeneca UK and the global company about the arrangements for the advisory board held on 10 November 2017 right up to the meeting taking place. The UK company did not want to certify the meeting due to concerns about the number of AstraZeneca representatives attending. The email at issue dated 8 November 2017 from a senior UK medical department employee was an attempt to overcome this issue. The email included three options in order to enable the advisory board to go ahead. The Appeal Board noted AstraZeneca agreed that the email of 8 November 2017 was poorly worded. The email referred to ensuring the company did not attract an audit and mentioned a self-report to the ABPI if the meeting went ahead as planned. The Appeal Board noted the submission from AstraZeneca that the senior UK medical department employee was new; and that the self-report was in relation to the breach of the company's SOPs and not in relation to the ABPI Code. The Appeal Board considered that the reference to self-report appeared to be in relation to the Code. The Appeal Board noted that the email of 8 November 2017 had been copied to several senior AstraZeneca members and queried why nobody had replied to the email to raise their concerns. AstraZeneca stated that there had been a discussion about the email at the time but there was no written record. Although there was no requirement to self-report, the Appeal Board queried why the company had not self-reported a breach of the Code at this point. This was said by AstraZeneca to be an oversight.**

**The Appeal Board considered that when submitting a response, companies need not include everything however the company had not provided the relevant source material it used in summarising events. The email of 8 November 2017 was clearly central and relevant to this case and did not appear to be consistent with the summary provided. In the Appeal Board's view to not submit the email was inexplicable. Effective self-regulation required companies to be open and transparent when responding to complaints; they had a duty to disclose all relevant documents and information. When compiling its response to the complaint AstraZeneca stated that it had referred to emails. The Appeal Board was not satisfied with AstraZeneca's submission as to why it had not provided the email dated 8 November when responding to the complaint.**

**The Appeal Board considered that the email of 8 November 2017 was clearly relevant and should have been provided to the PMCPA as part of AstraZeneca's response. Notwithstanding AstraZeneca's submission that it now had updated its processes, the Appeal Board noted that self-regulation relied, *inter alia*, upon the provision of complete and accurate information from pharmaceutical companies.**

**The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, AstraZeneca should be publicly reprimanded for failing to provide complete and accurate information in an open and transparent way.**

**The Appeal Board was concerned to note that AstraZeneca was also publicly reprimanded in 2016 by the Appeal Board for providing inaccurate information to the Panel (Case AUTH/2793/9/15).**

**The Appeal Board noted the Panel's comments above regarding AstraZeneca's conduct in responding to complaints. The Appeal Board noted its concerns about AstraZeneca's compliance culture. The Appeal Board gave consideration to the imposition of further sanctions including whether an audit should be required. However, on balance, the Appeal Board decided that no additional action was required.**

An anonymous, non-contactable complainant, who described him/herself as an employee of AstraZeneca UK Limited's marketing company, complained about compliance at AstraZeneca. The complainant referred to global activities and referred to an advisory board meeting held in 2017.

**COMPLAINT**

The complainant alleged that despite stating that one of AstraZeneca's values was 'we do the right thing', over the last five years the company had become solely focussed on profits ahead of its ethical obligations. Over the last couple of years, the trend had reversed in the UK marketing company and the focus on achieving AstraZeneca's goals through the right means had returned. However, the same could not be said for AstraZeneca's global functions.

The complainant stated that as a UK company, and with many of the employees in the global functions based in the UK, AstraZeneca should comply with the Code for activities led by global. However, this was not so. Global functions did not receive appropriate training on the Code and did not have regular Code case updates as in the UK marketing company. Global functions believed that they did have to know or comply with the Code (sic) and only had to follow AstraZeneca global standards which were loosely based on the Code. The complainant understood that all staff working in areas that were covered by the Code should have comprehensive Code training.

Due to this, globally led activities were usually conducted in a manner which was not in line with the requirements in the Code. The complainant was aware of a recent global advisory board, held in October 2017, with over 15 external advisors and a similar number of AstraZeneca employees. This was sent to the UK marketing company for approval as UK health professionals were advisors. The nominated signatory refused to approve this due to the excessive number of people and the view that this was not a genuine advisory board. However, the UK marketing company was put under pressure to approve this and the two other staff (roles named) in the UK told the nominated signatory to approve the advisory board, even though they acknowledged that it was likely to be a breach of the Code.

The complainant stated that there were likely to be a number of other global activities that were in breach of the Code but that AstraZeneca UK was not aware of them. The complainant asked that the PMCPA investigate this in order that the reputation of AstraZeneca and the wider pharmaceutical industry was not tarnished.

When writing to AstraZeneca, attention was drawn to the requirements of Clauses 2, 9.1, 14.2, 16.1, 18.1 and 23.1 of the Code.

**RESPONSE**

AstraZeneca submitted that it took compliance with all applicable laws and regulations very seriously, including pharmaceutical industry codes of practice. AstraZeneca believed that it had, at all times, addressed the advisory board referred to in the complaint in accordance with the high standards expected of a pharmaceutical company.

AstraZeneca was disappointed that the complainant had brought his/her concerns to the PMCPA rather than raising them internally. AstraZeneca noted that its commitment to ethics included training all staff on induction, and annually thereafter, on its internal escalation processes which also included details of its AZethics line, an externally hosted confidential online and telephone helpline, available 24 hours a day, 7 days a week. Whilst AstraZeneca did not deny the complainant's right to complain to the PMCPA, it was very important to note the reporting system which existed and to reiterate that AstraZeneca made every effort to encourage employees to report concerns and gave them a confidential route to do so. AstraZeneca submitted that it did this, because it was the right thing to do and because it was committed to continuous improvement across its organisation.

AstraZeneca refuted the complainant's general and unsubstantiated allegations about interactions between AstraZeneca's global and UK commercial functions and the general attitude of the global functions to compliance. As recognised in the complaint, 'Do the Right Thing' was one of AstraZeneca's five core values and underpinned all of its decisions. Like any organisation, there would always need to be discussions between colleagues to understand the implications of the underlying legal and regulatory requirements. It was grossly inaccurate to state that such discussions showed a disregard for the Code or a desire to put profit before compliance. The allegations suggested that the complainant did not have full insight into all the relevant and key discussions that took place about the advisory board, and did not have sufficient knowledge and experience of the organisation especially in relation to global processes.

AstraZeneca submitted that the only specific allegation related to an advisory board. Although the complainant did not specify a date, AstraZeneca

believed that the advisory board to which he/she referred was the Global Dapagliflozin T1D Indication Advisory Board held in Amsterdam from 9.30am to 5.30pm on 10 November 2017. AstraZeneca submitted that this advisory board was conducted in a compliant fashion.

**Issues to be addressed by the advisory board**

AstraZeneca stated that as part of its commitment to science, it had recently conducted the DEPICT-1 and DEPICT-2 studies to investigate the efficacy and safety of the selective sodium-glucose co-transporter 2 (SGLT2) inhibitor, dapagliflozin (Forxiga) in patients with inadequately controlled type 1 diabetes. This was a new area of potential application for this class of product and relied on a mode of action which had not previously been used in type 1 diabetics.

The advisory board was arranged by AstraZeneca's global medical affairs team. Global medical affairs looked to inform AstraZeneca's decision on an application for a potential new indication (US and EU) by gaining insight from key opinion leaders on the benefit/risk profile of Forxiga based on DEPICT-1 and DEPICT-2. The detailed objectives of the meeting were set out in a form for health professionals (copy provided).

The advisory board was a single advisory board required for insight gathering only. It was not part of a series.

**Selection and invitation of participants**

AstraZeneca selected the participants based upon:

- expertise and experience in the management of type 1 diabetes and its complications;
- experience with SGLT2 inhibitors and/or familiarity with diabetic ketoacidosis;
- the need to represent a diversity of advisor roles across the diabetes therapy area; and
- the need for representation from relevant geographies.

In order to meet the requirements, AstraZeneca selected seventeen potential participants. They were emailed by a global medical leader within global medical affairs in order to ascertain whether they were available (example email provided). A follow-up email invitation was sent by a third party agency based on confirmation of participant availability (copy provided).

**Number of health professionals attendees and compensation**

AstraZeneca stated that sixteen participants attended the advisory board. Compensation was paid to each in accordance with relevant local guidance and details were provided. It submitted that the compensation paid to the two UK health professionals was reasonable and in accordance with the UK marketing company's fair market value guidance.

**Agenda and materials**

Copies of the advisory board agenda, the presentations and the participants' pre-reading material were provided. AstraZeneca referred to the audio recording of the advisory board captured by the third party agency for the sole purpose of consolidating a report of the meeting.
The materials associated with this advisory board (agenda, presentations and discussion guide) were examined by a global medical affairs signatory in line with the requirements of the Code for non-promotional activities, and also a host country nominated signatory to ensure local host country regulations were adhered to.

**Feedback from participants**

There was no feedback form. Whilst AstraZeneca often sought feedback from attendees at its educational and promotional meetings, it was not standard practice to seek feedback from advisory board attendees.

**Selection and attendance of AstraZeneca staff**

Noting differences between the global and local standard operating procedures (SOPs), a compromise was agreed that only AstraZeneca attendees with a meeting relevant role were to be in the actual meeting room. Colleagues with a secondary requirement were allowed to listen remotely. Nine AstraZeneca staff were in the room along with 2 employees of the third party agency. A further three AstraZeneca staff listened to the advisory board from an adjacent room with a video link, together with a further 2 agency employees. AstraZeneca provided a rationale for attendance of its staff.

**Discussions concerning AstraZeneca attendees**

Discussions about the differences between the global and UK SOPs for advisory boards took place between global medical affairs and UK marketing company staff, in particular around the more prescriptive limit on the number of internal attendees that ordinarily applied under the UK SOP. Copies of both SOPs were provided. AstraZeneca submitted that neither of the two staff whose roles were mentioned by the complainant considered that the meeting was in breach of the Code. Furthermore, they did not pressurize the UK signatory to certify the meeting arrangements and AstraZeneca had found no evidence to the contrary. Team members confirmed that the one of these roles had made it clear on more than one occasion that AstraZeneca did not expect individuals to sign off any materials if they were not comfortable to do so. The UK nominated signatory confirmed that the two members of staff did not pressurize him/her to certify the meeting arrangements.

The advisory board was designed in line with AstraZeneca's relevant global SOP which AstraZeneca submitted was in accordance with the principles of the ABPI Code. The global SOP required adherence to local requirements including,

where appropriate, the need for local approval of matters relating to the attendance of local health professionals. As two UK health professionals were to attend this advisory board, the global medical affairs team approached local UK marketing company signatories to arrange certification for their attendance. The local UK marketing company signatories reviewed the advisory board and requested that certain changes be made, including in relation to the number/role of attendees: discussions on the changes took place over a number of weeks following the submission of the advisory board for review by the local signatory on 24 October 2017. Eventually, only a request from the UK signatories to change the number of internal attendees present in the meeting in order for the arrangements to be certified under the UK SOP remained under discussion. They presented several options to resolve this, one of which was the option eventually settled upon. Unfortunately, although it was agreed and an amended health professional form submitted by the global medical affairs team for approval on 9 November, they were not able to make a further resubmission of the health professional form before close of business that day owing to additional editorial changes to the form requested by the UK marketing company signatory. As a result, the UK signatory decided that it would not be appropriate to certify the arrangements of the advisory board on the following day (10 November) as the UK health professionals had already travelled and the activity had commenced: to do so would have been viewed as a retrospective certification. The UK signatory did not inform his manager of the lack of certification due to this timing issue until after the advisory board had started. This had been logged as a deviation and would be addressed in accordance with AstraZeneca's standard procedures for dealing with specific deviations.

**Training of global personnel**

AstraZeneca refuted the complainant's non-specific allegations concerning the level of training of global employees in the requirements of the Code; such allegations appeared to overlook the comprehensive training program in place for all staff across a wide range of topics, including regulatory compliance.

AstraZeneca maintained a web-based software solution to schedule and distribute training to staff based on their role, location and responsibilities. Various topics, including those related to medicines' promotional regulations, were made available to global employees on the network and these interactive modules allowed employees to work through training presentations on their own with trackable progress. An example of one, the training on scientific exchange was provided.

In addition, the global nominated signatories (GNSs) were tasked to train relevant global teams on topics related to the regulation of the promotion of medicines and their assigned therapy areas. Examples of summaries of such trainings were provided. All members of the GNS team were either UK registered pharmacists or registered physicians and they were registered with the Medicines and Healthcare products Regulatory Agency (MHRA) and PMCPA in line with Clause 14.4 of the Code. The majority had had extensive experience working in the medical affairs departments of UK pharmaceutical companies, and so had a deep understanding of the requirements of the Code. In addition, GNSs underwent robust training when they joined the company, and actively took part in various learning initiatives on the job to keep their knowledge up-to-date.

The AstraZeneca team used a variety of techniques to deliver training and these were reviewed regularly to ensure that training was up-to-date and effective. One of the methods used was WebEX for group training, called 'Nom Sig On- Air Sessions'. During these sessions, participants from global and affiliate countries dialled in to receive live audio training and follow visual presentations on their computer screens. The participants interacted with the presenters through the audio function or via webchat, with training sessions recorded to allow for easy make-up for employees who missed the group training or as useful on-demand refresher training. An example of a 'Nom Sig On-Air Session' on running a patient advisory board was provided.

AstraZeneca also used multimedia for training, typically videos that were widely available to all employees, not just those involved in the production and review of materials subject to the Code. These videos were mostly about 3 minutes each and provided succinct guidance. They allowed employees to build sufficient knowledge to know when they might be carrying out a regulated activity. An example of a transcript for one of the videos was provided.

**Clause 14.2**

AstraZeneca was disappointed that the arrangements for the attendance of the UK health professionals at the advisory board were not certified before it commenced, despite the scrutiny that was applied to this advisory board. AstraZeneca acknowledged that it did not meet the requirements of Clause 14.2 but noted that the failure to certify was based on a timing issue rather than a disregard of the requirements of the Code or the activity not being in accordance with the Code.

**Clause 16.1**

Given the extensive training regime described above, AstraZeneca denied a breach of Clause 16.2, whether generally in relation to the staff within global medical affairs or more specifically with relation to the staff involved in the advisory board.

**Clause 18.1**

The advisory board was appropriate and the remuneration provided to the health professionals represented a fair market value for their work, in accordance with AstraZeneca's internal guidance on fair market value. AstraZeneca denied any breach of Clause 18.1.

**Clause 23.1**

AstraZeneca denied any breach of Clause 23.1. In particular, the UK health professionals in question:

- had signed appropriate written contracts in respect of the advisory board;
- were selected based on appropriate criteria in order to enable AstraZeneca to fulfil a legitimate business need;
- were part of an appropriately sized group of health professionals contracted to provide the breadth of advice reflecting the scope of disease, complications of treatment and variation in geography for a global investment decision and
- were paid the fair market value for the services that they provided and were not hired as an inducement to prescribe.

**Clause 9.1**

Whilst AstraZeneca acknowledged and regretted the breach of Clause 14.2 referred to above, it did not accept that it failed to maintain high standards. The detailed discussions that took place over this one advisory board were a sign of the efforts that the company had made to maintain high standards.

**Clause 2**

AstraZeneca denied any breach of Clause 2. AstraZeneca believed that it had maintained high standards throughout and that the evidence demonstrated its commitment to upholding the reputation of the industry.

In summary, AstraZeneca stated that the advisory board was carried out for a legitimate business purpose, the arrangements were appropriate including a reasonable number of participants and AstraZeneca staff to achieve the stated business objectives. A difference in opinion based on variation in the UK and global SOPs was appropriately escalated and no pressure was put on the nominated signatory to approve an activity with which he/she was uncomfortable. Nevertheless, AstraZeneca accepted that the arrangements for the advisory board were not certified because the final amended forms were not submitted early enough for the UK signatory to certify them. However, AstraZeneca denied any other breach of the Code.

**FURTHER INFORMATION FROM ASTRAZENECA**

The Panel requested further information.

With regard to the changes to the arrangements for the advisory board requested by UK signatories, AstraZeneca submitted that during the initial review of travel arrangements for the two UK health professionals invited to attend the advisory board, the only point raised by UK signatories which required further discussion related to the number of AstraZeneca employees invited to attend the meeting and the need to clarify the rationale for their attendance. UK signatories requested that the internal attendee numbers be revised in line with requirements of the local UK SOP for advisory boards. This was in contrast to the global SOP which was not prescriptive regarding specific attendee numbers or ratios, but gave guidance to ensure the number of internal attendees was the minimum required to meet the objectives of the meeting. The ensuing discussion between global medical affairs and the UK focused on how to resolve the conflicting guidance. The compromise reached was to reduce the number of AstraZeneca attendees in the main room where the discussion was taking place during the morning session, with 5 staff members listening in from another room.

Once internal attendee numbers were agreed, the UK signatory requested the following additional changes, which were mostly editorial in nature, before final approval could be granted:

- a correction of an error which marked one of the UK health professional's fee for service as being outside acceptable fair market value limits when in fact it was within the limits;
- a request to attach the biography for one of the UK health professionals;
- a request to correct errors in the flight details for both UK attendees to accurately reflect the travel arrangements;
- a request to clarify job/role descriptions of AstraZeneca attendees and
- a request to clarify the final number of internal attendees.

With regard to the differences between AstraZeneca's letter of response and enclosed rationale for attendance of active AstraZeneca participants, AstraZeneca stated that a final internal preparatory meeting for the advisory board was conducted by global medical affairs on the day before the meeting. At that meeting, those present determined that two members of staff who had been due to listen from the neighbouring room would need to be in the main meeting room in order to answer questions and clarify points as part of the morning discussion. As a result, it was decided that three additional AstraZeneca employees would be present in the room as well. Although this increased the total number of AstraZeneca attendees inside the room to nine, AstraZeneca submitted it needed to exercise a degree of flexibility on this occasion to fulfil the requirements of the advisory board. About half way through the morning session, there was a problem with the listening device which led to the three remaining AstraZeneca participants joining the others in the main room until the end of that session.

Twelve AstraZeneca staff participated to facilitate the needs of the afternoon sessions which were split by region into the US and EU/International sessions. A list of advisors, AstraZeneca attendees and agency staff at each session was provided.

AstraZeneca stated that the welcome coffee was time allocated for coffee to be served outside the meeting room whilst advisors arrived. All twelve AstraZeneca attendees arrived at different times during the welcome coffee. No formal introductions or discussions took place between AstraZeneca staff and the advisors, most of whom used this time to

settle in or catch up with their colleagues or prepare for the meeting.

AstraZeneca stated that emails to ascertain availability to attend the advisory board were sent to one UK health professional on 25 September 2017 and to the other on 3 October 2017. These emails did not constitute formal invitations to attend the advisory board. It was important to clarify that whilst this contact was prior to formal UK signatory involvement, the purpose and nature of this contact was purely to ascertain availability; this communication was appropriate and compliant because it did not contain any substantive content.

The global medical affairs team engaged the UK signatory team to approve attendance of the UK attendees on 24 October 2017, after receiving confirmation of availability to attend. No formal invitation was sent to either UK health professional prior to involvement by UK signatories.

A formal invitation to attend the advisory board was sent to both UK health professionals on 6 November 2017.

A copy of correspondence sent with pre-read materials was provided.

The outcome and recommendations by the advisors were captured by the agency staff. The form containing the details of the information captured was provided. AstraZeneca submitted that this information clearly demonstrated a legitimate need for the advisory board, with relevant content, an appropriate agenda and aligned outputs.

AstraZeneca remained comfortable that the advisory board was entirely appropriate and that it was conducted in compliance with the ABPI Code.

**PANEL RULING**

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the Prescription Medicines Code of Practice Authority stated that anonymous complaints would be accepted but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The Panel noted that the parties' accounts differed; the complainant had provided no evidence to support his/her allegations and could not be contacted for more information.

With regard to the allegations about training staff, the Panel noted that AstraZeneca distributed training to staff based on their role, location and responsibilities. Various topics including those related to medicines' promotional regulations were made available to global employees on the AstraZeneca network allowing them to work through training presentations on their own with trackable progress. The example training for scientific exchange, medical education and sharing off-label information was dated March 2015. Other training for global nominated signatories to use when training relevant global teams was a one-page summary on medicines promotion regulations. There were three versions for the different audiences, medical personnel, marketing personnel and communications personnel. The training for nominated signatories appeared to be more detailed. The screen shot provided dated September 2016 listed 10 training modules with links to AZlearn modules. The patient advisory board training was undated.

The Panel noted that although the materials provided did not demonstrate comprehensive training on the ABPI Code, Clause 16.1 required relevant personnel concerned in any way with the preparation or approval of material or activities covered by the Code to be fully conversant with the Code and the relevant laws and regulations. AstraZeneca provided training to global staff and more detailed training to the nominated signatories who, as required by the supplementary information to Clause 14.1, Suitable Qualifications for Signatories, must have an up-to-date detailed knowledge of the Code. The Panel did not consider that there was evidence to show that on the balance of probabilities, AstraZeneca had not trained relevant global staff as alleged. The Panel therefore ruled no breach of Clause 16.1 of the Code.

Turning to the allegations about the advisory board, the Panel noted that it was acceptable for companies to pay health professionals and others for relevant advice. Nonetheless, the arrangements for such meetings had to comply with the Code, particularly Clause 23. To be considered a legitimate advisory board the choice and number of participants should stand up to independent scrutiny; each should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the advisory board. The number of participants should be limited so as to allow active participation by all. The agenda should allow adequate time for discussion. The number of meetings and the number of participants should be driven by need and not the invitees' willingness to attend. Invitations to participate should state the purpose of the advisory board meeting, the expected advisory role and the amount of work to be undertaken. If an honorarium was offered it should be made clear that it was a payment for such work and advice. Honoraria must be reasonable and reflect the fair market value of the time and effort involved.

The Panel noted that the agenda for the advisory board included in the presentation started with a welcome coffee from 9.30am until 10.30am and the actual advisory board started at 10.30am and ended at 5.30pm; there were breaks for lunch and tea. It was held in Amsterdam and was co-chaired by the external speaker and a member of AstraZeneca staff. One of the two speakers in the morning session was from AstraZeneca and the moderators for the afternoon discussion groups were both from AstraZeneca.

The initial invitation to one of the UK participants was provided (dated 25 September 2017). The initial invitation to the other UK participant (dated 29 September 2017) was provided following the Panel's request for further information.

The invitation described the advisory board as part of AstraZeneca's ongoing commitment to supporting health professionals and patients. The objective of the meeting was to gain expert feedback and insights on the role of SGLT2 inhibitors in type 1 diabetes and specifically the DEPICT programme studies.

The invitation to the external speaker set out the objectives as to critically evaluate the benefit/risk of dapagliflozin on type 1 diabetic patients and to provide recommendations for safe and effective use of dapagliflozin in type 1 diabetes.

The pre-reading consisted of 6 published papers including the 'American Association of Clinical Endocrinologists and American College of Endocrinology Position Statement on the Association of SGLT-2 Inhibitors and Diabetic Ketoacidosis' and the published DEPICT study. It was sent to the UK participants on 4 November 2017. The email of 4 November referred to the recipient already receiving details of how to register for the meeting. The official invitation was sent on 6 November and this asked the participant to register for the meeting.

There were 78 slides to be used during the day. Twenty-eight slides were presented in the first session by an external speaker, one of the investigators of the DEPICT studies. This one-hour session, which focused on the results of the two studies and their clinical interpretation, included two periods for discussion. The second session of seventeen slides, presented by an AstraZeneca employee, focused on the safety results of the two studies and lasted for one hour and fifty minutes. In the afternoon the group was split into two (US and EU/International) and each group, moderated by AstraZeneca, discussed as session 3 (45 mins) the efficacy results, in a 'Focused discussion on efficacy elements including $HbA_{1c}$, weight and continuous glucose monitoring'. Session 4 (90 minutes) was a discussion of the benefit/risk of dapagliflozin in type 1 diabetes patients in particular 'Guidance on insulin dose reduction, dose response 5mg vs 10mg dapagliflozin, special precautions, patient subgroups, labelling'. The day ended with 30 minutes for summary and closing remarks. The short agenda provided included the sub heading 'Group discussion is 80% or more of each allocated session time and includes all participants'.

The Panel queried whether so many slides were needed on the DEPICT outcomes given the pre-reading included the published studies.

The Panel noted that the advisory board was to help AstraZeneca decide about an application for a new indication in the US and EU. In that regard, seven of the 16 advisors were from the US, eight came variously from five European countries (two from the UK, a doctor and a diabetes specialist nurse) and one advisor was from Israel. In addition, there were 12 AstraZeneca staff.

The rationale for the attendance of AstraZeneca staff was provided. This indicated that the meeting ran from 9.30 until 17.30 whereas the first hour was spent on a welcome coffee with the advisory board starting at 10.30. The stated business justification was to present and discuss DEPICT-1 and -2 data, to critically evaluate benefit/risk of dapagliflozin on type 1 diabetes patients and to provide recommendations for the safe and effective use of dapagliflozin in type 1 diabetes. The business justification in this document was different to the objectives provided to the attendees. This document listed the names of the 12 AstraZeneca staff and their role as well as the rationale for their attendance. Five of the staff were to watch the first part of the advisory board in a separate room on video link and then three would actively participate in the breakout sessions. This was different to the submission from the company which stated that 9 AstraZeneca staff joined the meeting and three listened in another room. The further information from the company stated that on the day there were 9 AstraZeneca staff in the room and the three listening in another room joined the main room about half way through the morning session due to a technical problem.

From the list of AstraZeneca attendees four were assigned to participate in each of the breakout sessions; it was not stated if the other four were to participate in either session or not. The further information confirmed that all 12 AstraZeneca staff participated in the afternoon breakout sessions.

It was not clear to the Panel why AstraZeneca had not described what actually happened at the advisory board in its first letter of response. It was unacceptable and concerning that details of the arrangements for AstraZeneca staff attendees were only provided following a request for additional information.

The AstraZeneca UK marketing company guideline, 'UKMC Advisory Board Standard' stated that an advisory board should generally consist of no more than 10 advisors and that generally no more than 3 AstraZeneca employees might attend. Additional employees might attend only if they could show a legitimate and documented need.

The Panel was concerned about a number of aspects of the advisory board including the number of AstraZeneca attendees which was well outside the UK SOP. However, this did not necessarily mean that the advisory board failed to meet the requirements of the ABPI Code.

The Panel was concerned to note, given the compliance difficulties that companies could experience with advisory boards and the high profile given to such in the UK recently, that it appeared that the arrangements for the meeting were only submitted for local review on 24 October– only 12 working days before the meeting took place. The Panel was also concerned that the day before the advisory board AstraZeneca was making fundamental changes to the arrangements and increasing the number of AstraZeneca staff in the meeting room. In the Panel's view, the timescales and last minute changes would put unnecessary pressure on the nominated signatory to approve a meeting for which all of the arrangements should have already been in place; the UK SOP stated that material should be submitted for approval at least 6 weeks before the meeting date.

The Panel noted that no evidence was supplied in relation to the alleged pressure on the UK signatory to certify the meeting. The Panel was concerned as this was a serious allegation and it was vital that signatories were free to decline certifying material if in their opinion it did not meet the relevant requirements of the Code. It appeared from AstraZeneca's submission that there was discussion between the UK company and the global company. This was particularly concerning given that this was ongoing so close to the date of the advisory board and that advisory boards were high risk area for companies. The Panel queried whether the certification should have been completed before the UK advisors were first approached at the end of September. If the arrangements were not capable of certification, UK health professionals should not have been approached.

The Panel noted that the advisory board which was held outside the UK and involved UK delegates had not been certified. The Panel noted AstraZeneca's submission that this was due to a timing issue rather than because the signatory was concerned with compliance with the Code. The Panel ruled that the failure to certify was a breach of Clause 14.2 of the Code as acknowledged by AstraZeneca.

The Panel noted the complainant alleged that the advisory board was not genuine. No evidence had been provided by the complainant who had not clearly identified the advisory board about which he/she was concerned. As noted above, the Panel was concerned about the advisory board identified by AstraZeneca but did not consider that the complainant had shown, on the balance of probabilities, that the advisory board held on 10 November 2017 failed to meet the requirements of the Code and thus that any payment was inappropriate. Thus, the Panel ruled no breach of Clauses 23.1 and 18.1.

On balance, the Panel considered that the arrangements for certification and the short time frame increased the pressure on UK certifiers. This and the failure to certify meant that AstraZeneca had failed to maintain high standards. The Panel ruled a breach of Clause 9.1 of the Code.

Noting its rulings above the Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such use. The Panel therefore ruled no breach of Clause 2.

**CASE AUTH/3013/1/18 – ADDENDUM**

Following completion of this case in April 2018 and its publication on the PMCPA website in May 2018 a letter was received in June 2018 regarding the case and providing further information. It appeared to have come from the original anonymous, non-contactable complainant, who had described him/herself as an employee of AstraZeneca UK Limited.

The letter appeared to provide information which had not been provided by AstraZeneca in its response to the complaint. The author of the letter referred to an email from a senior UK medical department employee outlining options to deal with the advisory board in question. AstraZeneca referred to 'several options' in its response to the PMCPA but this was not expanded upon nor did the PMCPA question this. The author of the letter stated that one of the options was 'proceed as planned, log this as a breach and consider whether to self report to the ABPI'. The distribution of the email included several senior members of AstraZeneca's UK and Global teams.

The author of the letter referred to AstraZeneca's response to the PMCPA which referred to 'Do the right thing' underpinning all its decisions, however none of the senior people in the email distribution responded to the email to say that proceeding with an advisory board that was considered to be in breach of the Code was unacceptable and not the right thing. It was also noticeable that the senior medical department employee was not concerned about complying with the Code or 'doing the right thing' but rather 'trying to ensure we do not attract an audit' (presumably from the PMCPA).

The author of the letter pointed out that AstraZeneca in its response to the complaint stated that named staff did not believe that the advisory board was in breach of the Code. In the author of the letter's view, the email clearly demonstrated otherwise. In addition, AstraZeneca's failure to disclose the email in response to that case and give complete and accurate information to the PMCPA demonstrated that AstraZeneca did not take self-regulation seriously. Furthermore, that senior employees were already aware of the issues and were happy to proceed without making changes to the advisory board and make a voluntary admission later, meant that it was not appropriate to raise concerns using internal channels, as stated by AstraZeneca in its response.

Given the PMCPA appeared to take a grave view of companies that did not respond in full to complaints, the author of the letter asked the PMCPA to look again at this case as a matter of urgency, stating that '…surely AstraZeneca's conduct is not acceptable?'. There had already been two cases ruled in breach of the Code in 2018 and as long as this unacceptable culture existed, particularly amongst senior employees, then there was likely to be further breaches of the Code.

The matter was taken up with AstraZeneca which was asked to comment on a number of matters including Case AUTH/2793/9/15 where additional information was provided following the completion of a case.

AstraZeneca was advised that on receipt of its response the PMCPA would consider the position. The Appeal Board would have to be informed and this might be by way of a report under Paragraph 8.2 of the Constitution and Procedure.

**RESPONSE FROM ASTRAZENECA**

AstraZeneca reiterated its firm commitment to compliance with all applicable laws and regulations, pharmaceutical industry codes of practice, including upholding effective self-regulation. It had fully

accepted the breaches of Clauses 9.1 and 14.2 ruled in Case AUTH/3013/1/18 and listed the steps already taken to address the issues raised.

AstraZeneca acknowledged the PMCPA's concern regarding the completed cases (Case AUTH/3011/1/18, Case AUTH/2793/9/15 and Case AUTH/3013/1/18). The company submitted that it made every effort to respond to the PMCPA in good faith and to the best of its knowledge at the time but recognised the continuing need to review the complexity and efficiency of its ways of working between Global and the UK Marketing Company. Whilst it was extremely disappointed that these incidents occurred, AstraZeneca submitted that the compliance governance framework between the UK Marketing Company and Global teams remained effective.

AstraZeneca referred to its response in Case AUTH/3013/1/18 in which the discussions in relation to the advisory board were outlined:

> 'The local UKMC signatories reviewed the advisory board and requested that certain changes be made, including in relation to the number/role of attendees: discussions on the changes took place over a number of weeks following the submission of the Ad Board for review by the local signatory on 24th of October 2017. Eventually, the one remaining change under discussion was a request from the UK signatories to change the number of internal attendees present in the meeting in order for the arrangements to be certified under the UK SOP. They presented several options to resolve this, one of which was the option which was eventually settled upon.'

AstraZeneca submitted that the email provided by the author of the letter represented a snapshot of these discussions and, in its view, was consistent with the description of them as set out above. In addition, AstraZeneca's further response in Case AUTH/3013/1/18 provided specific information on the acceptance of option 1 as referred to in the email:

> 'The ensuing discussion between the Global Medical Affairs (GMA) team and the UK team focused on how to resolve the conflicting guidance. The compromise reached at this time was to reduce the number of internal AZ attendees in the main room where the discussion was taking place during the morning session, with 5 of the internal attendees listening in from another room.'

Discussion, questioning and challenge were integral parts of reaching the right outcome for all compliance activities under the Code.

AstraZeneca stated that it was important to note that at no point throughout ongoing discussions was the legitimacy of the advisory board called into question: the discussions and opinions were centred around a potential procedural breach of the AstraZeneca UK Marketing Company SOP arising from a conflict with the Global SOP. This email formed part of that on-going discussion and could be misinterpreted when taken out of context. The language was aimed solely for internal dialogue with an audience which was largely aware of the issues and the discussions. AstraZeneca confirmed with its senior UK medical department employee director that he/she was ostensibly referring to the fact that it was technically possible for the global organisation to proceed with the meeting in breach of the UK SOP but, in such an event, it would be necessary to review the question of whether this could then lead to a breach of the Code which would have to be self-reported. The senior UK medical department employee took it that it would be self-evident to the internal audience that this option was to be avoided.

AstraZeneca submitted that in hindsight, the email was vulnerable to misinterpretation by those not involved closely. As a result, AstraZeneca would commit to providing more training to staff on the importance of using clear, unambiguous language in the future to reduce any potential miscommunications. AstraZeneca would continue to support and empower its employees to seek clarity on any concerns they might have.

The email represented a snapshot in time of the discussions held between the AstraZeneca UK Marketing Company and the Global Medical Affairs team prior to the advisory board taking place, which resulted in a suitable resolution being reached for the advisory board to proceed in full compliance with the Code. Therefore, AstraZeneca respectfully believed that the email provided did not provide additional information or change AstraZeneca's position for the Case AUTH/3013/1/18.

AstraZeneca maintained that the advisory board at issue in Case AUTH/3013/1/18 was carried out for a legitimate business purpose and the query raised did not at any stage question the legitimate purpose of the advisory board. Further to the ongoing discussions, the number of proposed AstraZeneca attendees had been satisfactorily resolved, and such resolution allowed AstraZeneca to proceed with the advisory board in good faith. Therefore, a voluntary admission was not considered because the concerns had been satisfactorily addressed and such an admission was not required.

The company stated that it would be reviewing the discrepancy concerning AstraZeneca attendee arrangements internally in line with its processes.

AstraZeneca submitted that the email provided had been taken out of context and did not accurately reflect the full discussions that had taken place. AstraZeneca was concerned that the allegations, based on an isolated email being misrepresented, might be the result of an employee with an intention of harming AstraZeneca's reputation.

In summary, AstraZeneca submitted that the information received by the PMCPA following the completion of Case AUTH/3013/1/18: Global advisory board was appropriately reflected in the initial and follow-up responses provided by AstraZeneca.

**REQUEST FROM PMCPA FOR FURTHER INFORMATION**

To help the Authority understand this matter, AstraZeneca was asked to address a number of points including other cases where governance was raised by the Panel. These being Case AUTH/2866/8/16 where the Panel referred to concerns about governance of speaker meetings activities, Case AUTH/2746/1/15 where a tweet by global had not been certified and Case AUTH/2969/8/17 where the Panel referred to representative's activities and the need for AstraZeneca to review its processes.

**RESPONSE FROM ASTRAZENECA**

AstraZeneca stated that it carried out a comprehensive review following receipt of the PMCPA letter and addressed each point including those about other cases where governance was raised by the Panel.

AstraZeneca stated it was fully committed to upholding high standards and compliance with all applicable laws and regulations, pharmaceutical industry codes of practice, including upholding effective self-regulation.

AstraZeneca was disappointed that the cases highlighted occurred and accepted that mistakes were made. However, such errors related to unusual individual facts. In the broader context of its substantial business activities in the UK, reflecting the fact that it was a UK head quartered company, AstraZeneca submitted that they were outliers, which did not reflect the totality of its culture and strong governance framework. In each case, AstraZeneca had reacted by taking measures to ensure that lessons were learnt, processes were strengthened and specific concerns were addressed.

In summary, AstraZeneca stated it had a robust governance framework in place which sought to identify, manage and prevent risks using three distinct lines of defence. Line managers played a critical role as the first line of defence, with a defined duty to promote a strong compliance and risk management culture, whilst ensuring that day to day risks were controlled and monitored on an ongoing basis. The compliance functions provided policy and standard setting, communication and training, advice and assurance as well as monitoring and auditing to ensure that the first line of defence remained fit for purpose and robust. The third line of defence, the internal audit function provided independent advice and assurance to senior management of the effectiveness of risk, first and second lines of defence.

As an organisation, AstraZeneca stated it continuously monitored progress and had continuous improvement initiatives to ensure the robustness of processes and culture of compliance. This was evidenced by the measures AstraZeneca put in place to address failings identified in each of the cases highlighted here and through its standard monitoring and audit processes.

In addition, the AstraZeneca UK Marketing Company had integrated all compliance-related decision making into a cross-functional compliance governance group (Ethics Xceed) in March 2018, comprising compliance, legal, medical, regulatory affairs and finance. The Group's role was to provide advice and guidance to the organisation on issues relating to compliance with the various regulations and provided further evidence of AstraZeneca's commitment to a strong governance culture.

AstraZeneca remained fully committed to maintaining high standards and effective self-regulation. It totally accepted and understood the need for a thorough investigation of the allegations made by the author of the letter dated 18 June 2018 but was concerned that the complainant had made sweeping allegations supported only by an email which had been used and quoted out of context. Although instances of Code-related breaches remain isolated, AstraZeneca was disappointed that any such cases had occurred and continued to strengthen its ways of working and processes to ensure that it continued to remain compliant with the necessary internal and external requirements.

With regard to the PMCPA's identification of six cases, (Cases AUTH/2746/1/15, AUTH/2793/9/15, AUTH/2866/8/16, AUTH/2969/8/17, AUTH/3011/1/18 and AUTH/3013/1/18) involving both AstraZeneca UK Marketing Company and the Global company over a period of some four years, AstraZeneca submitted it had provided full responses to all of the completed cases and demonstrated that these cases did not reflect a pattern, but were based on specific individual circumstance. Furthermore, it had shown that not only had it carefully considered the Panel's recommendations, it had taken all necessary action to address these and to effect changes to prevent recurrence. In the circumstances described, AstraZeneca respectfully suggested that a referral to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure was neither merited nor appropriate.

**FURTHER CONSIDERATION BY THE PANEL**

The PMCPA decided that the original Panel should reconvene to consider the matter in relation to Paragraph 8.2 of the Constitution and Procedure which provided that the Panel might report to the Appeal Board any company whose conduct in relation to the Code, or in relation to a new particular case before it, or because it repeatedly breached the Code such that it raised concerns about the company's procedures, warranted consideration by the Appeal Board. Such a report to the Appeal Board might be made notwithstanding the fact that a company had provided an undertaking requested by the Panel. The Panel noted that AstraZeneca had provided the requisite undertaking.

The Panel noted that the author of the letter had provided a copy to the Medicines and Healthcare products Regulatory Agency (MHRA) as the author was concerned there appeared to be no activity and alleging that AstraZeneca was receiving preferential treatment. The PMCPA responded to inform the MHRA that the matter had been followed up with AstraZeneca and would be considered by the Panel shortly. The delay was due to the number of

complex cases. AstraZeneca was not receiving any preferential treatment.

The Panel noted the difficulties for UK companies regarding activities run by global.

The Panel noted the email trail dated 7 and 8 November 2017 provided as additional information which appeared to provide context to the discussions between the UK company and the global company about the arrangements for the advisory board held on 10 November 2017. It was clear that the concerns raised by the UK went beyond just a difference between the UK and global SOPs. Reference was made to advisory boards being in the spotlight in the UK over the last 18 months, ever since the Astellas case. The MHRA had questioned the validity of advisory boards and that the UK position was rather sensitive at the moment due to the AstraZeneca cases at the Panel and that it was '… trying to ensure we do not attract an audit'. The senior UK medical department employee stated that the need for the global advisory board was clear and the agenda was reasonable. The ratio of AstraZeneca attendees to health professionals was high. The situation was described as low risk but if a complaint were made it would be marginal as to whether it could be defended from a perceptual perspective. Three options were proposed these being firstly that the extra 5 AstraZeneca attendees watched the first part of the advisory board in a separate room via a video link and then participated in the breakout sessions. Secondly to minimise the risk, reduce the number of AstraZeneca attendees to 8 (the ratio of just above 2:1 would still be inconsistent with the UK SOP). And thirdly to proceed as planned and capture it in the UK as a breach and then it could be discussed with the relevant UK team as to whether a self-report to the ABPI was needed. The email trail went on to state that the senior UK medical department employee wanted to avoid dropping the UK health professionals and also disrupting the plans for the proposed agenda. He/she was happy to go with any of the three options. He/she understood that this was frustrating but 'we do need to be consistent in our approach to implementing the code'. The email concluded that he/she would be working with the team to look at current SOPs to ensure that they continue to be compliant but were clear and not arduous to implement.

The Panel considered that it was not clear from the email trail whether the senior UK medical department employee considered that the number of AstraZeneca attendees at the advisory board was in breach of the Code or in breach of the AstraZeneca UK SOP. The email spelt out three options. The Panel noted that the company had decided on option 1 although as included in the report for Case AUTH/3013/1/18 this did not happen due to technical issues.

The Panel considered the email including the context of discussions about the advisory board and the perception of the email. The Panel considered that the reference to self-reporting was a possible reference to the need for AstraZeneca to consider making a voluntary admission about a possible breach of the Code. Clearly it was important that companies followed their SOPs but not doing so was not in itself necessarily a breach of the Code.

The impression of the email was that the UK company had concerns about the arrangements for the advisory board, in particular the number of AstraZeneca attendees. Full details about the number of AstraZeneca attendees had only been provided to the Panel considering the case when it asked for further information.

The Panel noted that clearly there were difficulties with the advisory board and breaches of the Code had been ruled and a number of concerns raised. At that time it was also clear that AstraZeneca had not provided all the information. In relation to AstraZeneca's submission that as the Panel had not asked for the email of 8 November it had not provided the email, the Panel noted that self-regulation relied on companies to provide all relevant material. As the Panel did not know of the existence of the email, it could not request it.

The Panel noted AstraZeneca's submission that the email represented a snapshot of the discussions that had taken place and these were explained in the company's response to Case AUTH/3013/1/18 where it stated 'they presented several options to resolve this, one of which was the option which was eventually settled upon'.

Now having received the email of 8 November the Panel did not consider that this additional information would have made a difference as to whether it thought the advisory board itself was in breach of the Code. The Panel had ruled no breach in this regard based on the complainant not having shown on the balance of probabilities that there was a breach of the Code. However, the new information which provided some insight into the company's compliance culture was a concern as was AstraZeneca's general approach with regard to providing information to the Panel as evidenced by the number of times over the last couple of years that the company had either not provided all the relevant information or had provided misleading information. This was set out in the Panel's request for further information from AstraZeneca.

Taken as a whole, the Panel considered that AstraZeneca could not clearly demonstrate its stated commitment to self-regulation in the broadest sense. It was concerned that actions might be taken by AstraZeneca so as to '… not attract an audit' rather than ensuring compliance with the Code and its own procedures. The Panel was also concerned that it appeared from the email and other aspects of the complaint that for some staff raising concerns about activities was difficult at AstraZeneca and this contributed to the differences of opinion between UK and Global. However, it decided that, on balance, the material before it, most of which had come to light either during the consideration of the cases or afterwards and had been the subject of a public reprimand, had been addressed and thus on balance a formal report to the Appeal Board was not needed at this stage. The Panel's view was that these examples should be reconsidered if there

were further instances of AstraZeneca failing to provide comprehensive information. The Appeal Board would be provided with details of the Panel's further consideration following a similar format to the details provided for cases which concluded at the Panel level.

**APPEAL BOARD CONSIDERATION OF CASE REPORT**

As the case completed at the Panel level the Appeal Board was provided with certain papers (the case report, Panel minutes, update to the case report, letter from the anonymous non-contactable complainant providing the email at issue dated 18 June 2018, and the correspondence with the MHRA. (Paragraph 4.1 of the Constitution and Procedure).

The Appeal Board considered that the additional information in this case raised serious issues including about the provision of incomplete and/or inaccurate information. The Appeal Board's view was that further consideration should be given to this matter including the possibility of imposing further sanctions under Paragraph 11.1 of the Constitution and Procedure.

AstraZeneca was advised that the Appeal Board was giving further consideration to this matter including considering imposing additional sanctions and asked to respond in writing, as well as be given the opportunity to attend the Appeal Board when the matter would be considered. AstraZeneca was provided with a copy of the papers.

**COMMENTS FROM ASTRAZENECA**

AstraZeneca submitted that in order for it to appropriately be represented it wanted more information on those specific matters which were of concern to the Appeal Board and which would be considered in that regard it noted that the Panel had made reference to Case AUTH/2793/9/15.

**RESPONSE FROM THE PMCPA**

The PMCPA advised AstraZeneca that the matters of concern to the Appeal Board were set out in its decision. The issues were set out in the Panel's consideration of the additional information. Various letters from the PMCPA and AstraZeneca's response referred to other cases:

Case AUTH/2538/10/12, Case AUTH/2746/1/15, Case AUTH/2793/9/15, Case AUTH/2866/8/16
Case AUTH/2969/8/17 and Case AUTH/3011/1/18.

**COMMENTS FROM ASTRAZENECA**

AstraZeneca submitted that it strongly disagreed with the Panel's characterisation of it. However, whilst it was disappointed by the Panel's consideration and the decision of the Appeal Board, it remained fully committed to the Code and the principle of self-regulation. AstraZeneca therefore welcomed the opportunity to discuss these issues with the Appeal Board.

**Background**

AstraZeneca set out the background including that in June 2018, the PMCPA received a further letter, attaching an email from a senior UK medical department employee describing available options in relation to the advisory board meeting, which had not been provided by AstraZeneca in its response to the original complaint. AstraZeneca submitted its detailed response above.

AstraZeneca noted that it had received no further correspondence or decision from the PMCPA until 10 May 2019, over 9 months later. The Panel's consideration concluded that the additional information would not have made a difference as to whether the advisory board was in breach of the Code and did not alter its previous ruling. However, as a result of the email from a senior UK medical department employee, the Panel raised various concerns in relation to AstraZeneca's compliance culture and the company's approach to the provision of information to the PMCPA.

AstraZeneca noted that the Panel had raised the following concerns:

- The UK company appeared to have concerns in relation to the arrangements for the advisory board organised by Global, in particular the number of AstraZeneca attendees. However full details about the number of AstraZeneca attendees had been provided to the Panel only when it requested further information.
- AstraZeneca's reason for not disclosing the email from a senior UK medical department employee of 8 November 2017 was that this had not been requested. However, self-regulation relied on companies to provide all relevant material; as the Panel had not been aware of the email it could not request disclosure.
- The Panel considered that the new information (ie the email of 8 November 2017), provided some insight into the company's compliance culture and was a concern.
- The Panel expressed concern in relation to AstraZeneca's general approach with regard to providing information to the Panel as evidenced by the number of times over the past couple of years that the company had either not provided all relevant information or had provided misleading information.
- Overall, the Panel considered that AstraZeneca could not clearly demonstrate its stated commitment to self-regulation in the broadest sense. It was concerned that actions might be taken so as not to attract an audit, rather than ensuring compliance with the Code and its own procedures. The Panel was also concerned that for some staff, raising concerns about activities was difficult at AstraZeneca and this contributed to differences of opinion between AstraZeneca UK and Global.

After considering the totality of the evidence, the Panel concluded that these matters had been addressed and that, on balance a formal report to the Appeal Board was not needed at this stage.

**AstraZeneca's response to the Appeal Board's concerns**

AstraZeneca submitted that the characterisation of its compliance culture and approach to the PMCPA was fundamentally incorrect. AstraZeneca would therefore demonstrate its commitment to a robust culture of compliance and respect for the Code both within the UK Marketing Company (UKMC) and across the Global organisation and address the specific issues that the Panel had highlighted.

AstraZeneca submitted that the matters identified by the Panel were not indicative of wider or systematic issues. One of five of AstraZeneca's core values was 'Do the Right Thing' and this underpinned how it conducted its activities and every decision that it made.

As a preliminary matter AstraZeneca reiterated that throughout Case AUTH/3013/1/18, the legitimacy and the business need for the advisory board itself was not in doubt and was not therefore, considered a breach of the Code. The advisory board was important to provide AstraZeneca key advice on Type 1 Diabetes, in addition, AstraZeneca had accepted the breaches associated with this case and as disclosed previously, had taken steps to address these as a UK and Global organisation.

AstraZeneca submitted that the PMCPA had stated that it had withheld information in two ways: firstly, by failing to provide the email dated 8 November 2017, and secondly, by having failed to disclose that technical issues had meant that the agreed arrangements for the advisory board had not been implemented in practice. AstraZeneca's detailed response to these matters was set out in its letter of 22 August 2018.

AstraZeneca submitted that in relation to the first issue, the Panel appeared to have misconstrued its comment that this email was not provided because it had not been requested. To be clear, AstraZeneca had never suggested that the email was not provided because this specific email was not requested but rather that AstraZeneca did not provide any emails because the PMCPA had asked it to provide details of the internal discussions that took place. Therefore, AstraZeneca had summarised the relevant discussions (verbal and written) in a manner which properly reflected the totality of those discussions. The complainant shared one email from the totality of the discussion and it had been positioned in a manner that was inconsistent with the context of the discussions; considering this email in isolation gave an incorrect impression of the overall email correspondence and created a misleading representation of AstraZeneca's culture. The Panel had effectively confirmed this where it noted that now having received the email of 8 November it did not consider that this additional information would have made a difference as to whether it thought the advisory board itself was in breach of the Code. Furthermore, AstraZeneca submitted that it would significantly increase the already substantial burden on companies and the PMCPA if companies were required to disclose all correspondence, even tangentially related to a complaint, in every case. AstraZeneca submitted that with respect to the second issue, it acknowledged that it was unfortunate that it was not able to disclose in its original response that the option that had been agreed between the UKMC and the Global teams could not be implemented on the day of the advisory board. As explained previously, this was not provided to the internal complaint management team as part of the original investigation. It was only as part of the second stage of the complaint [March 2018] that a member of the Global medical team recalled the internal meeting the day before the advisory board and technical issues on the day of the advisory board. AstraZeneca submitted that it had taken preventative actions to ensure full initial disclosure.

AstraZeneca submitted that as soon as its investigating team became aware that the advisory board had not been conducted in accordance with the agreed plan, due to the technical issues that occurred on the morning of the advisory board, this was passed on to the PMCPA in its submission of 15 March 2018. This indicated AstraZeneca's commitment to openness and transparency with the PMCPA rather than any systematic attempt to withhold information.

Finally, AstraZeneca submitted that whilst the Panel did not explain its particular concerns in relation to Case AUTH2793/9/15 and Case AUTH/3011/1/18, delayed disclosure in these cases resulted from the particular facts of those matters and did not reflect a deficiency in AstraZeneca's culture or approach. Case AUTH/2793/9/15 related to a leavepiece about how to create a clinical system search to identify patients suitable for treatment with Forxiga (dapagliflozin). Following a complaint, AstraZeneca provided information about the search arrangements, including details (which could not be verified by AstraZeneca) provided by the agency contracted by AstraZeneca for this work. The information provided by the agency turned out to be incorrect. While AstraZeneca accepted responsibility for the error of its agency, it strongly resisted any conclusion that this case demonstrated any deficiency in company culture in relation to disclosure of information during the self-regulation process.

AstraZeneca submitted that Case AUTH/3011/1/18, related to a press release issued in November 2017. In this case AstraZeneca did not fail to disclose information but rather acted in good faith to present its understanding that the applicable financial regulations prevented it from removing the press release from its website. AstraZeneca offered a solution that it thought would meet the needs of the Code and the financial regulations. When this solution was turned down by the PMCPA, it took external legal advice to determine if there was any way to satisfy both the financial regulations and Code requirements. It was determined this could be done by modifying and not removing the press release provided that the modifications did not have any financial implications. AstraZeneca then worked with its legal team to find an edit that would meet both sets of regulations. AstraZeneca contended this demonstrated its flexibility and willingness to find

solutions to meet the various regulations it operated under and underlined its value of doing the right thing. At the consideration of this matter the AstraZeneca representatives fully accepted the breaches of Clauses 14.2 and 9.1 ruled and remained disappointed that the arrangements were not certified, despite the scrutiny applied to the advisory board. Reassurance had been provided to the UK signatory team and confirmation on internal reporting routes. The UK had run a 'Speak Up' campaign during its regional compliance week. The global Advisory Board SOP had been revised, and training provided. Case AUTH/3013/1/18 was published and shared with all relevant staff. The UK Advisory Board SOP was currently being reviewed to ensure alignment with Global. Management of the investigation process had been strengthened and a clearer process for investigating cases involving both UK and Global had been agreed.

With regard to the non-disclosure of a senior UK medical department employee's email, AstraZeneca noted that the PMCPA had requested comprehensive details about the advisory board at issue and asked what internal discussions had taken place about the number of staff attending. The PMCPA had also requested specific documents as part of the initial complaint, but not email correspondence. AstraZeneca provided a summary of the discussions in the initial response to the complaint, as requested. The PMCPA had not objected to the summary. Following disclosure of the email by the complainant and additional context provided by AstraZeneca, the PMCPA found that the email did not alter its original ruling.

AstraZeneca submitted that the information provided in its initial response with regard to the number of AstraZeneca attendees was made in good faith. Upon further questioning, additional information was provided when Global colleagues recalled the precise arrangements on the day of the advisory board.

AstraZeneca accepted that the email was poorly worded but submitted that it was directed to an informed audience. The comment regarding audit referred to the fact that advisory boards were a sensitive area. The overall intent behind the email was to uphold compliance.

AstraZeneca submitted that the signatory did raise his/her concerns with senior medical and compliance colleagues.

In summary AstraZeneca submitted that the advisory board at issue was legitimate and the initial failure to provide accurate information concerning attendees was not deliberate or intentional. AstraZeneca's response was an appropriate summary of the totality of discussions as requested by the PMCPA. The email of 8 November 2017 was poorly worded but was not intended to suggest any disregard for the Code or for company procedures. It did not reflect a poor compliance culture. Actions had been taken to address these failings and to improve ways of working. The discussions that took place actually showed that individuals were free to raise concerns as a normal part of AstraZeneca's processes and culture. The additional cases identified by the PMCPA had their own particular facts and unique root-causes. Appropriate corrective and preventative actions (CAPAs) had been implemented.

**APPEAL BOARD CONSIDERATION**

The Appeal Board noted the Panel's rulings of breaches of Clauses 9.1 and 14.2 of the Code. The Appeal Board noted that the company had apologised and admitted that it had made errors.

The Appeal Board noted the context in that there had been discussions between AstraZeneca UK and the global company about the arrangements for the advisory board held on 10 November 2017 right up to the meeting taking place. The UK company did not want to certify the meeting due to concerns about the number of AstraZeneca representatives attending. The email at issue dated 8 November 2017 from the senior UK medical department employee was an attempt to overcome this issue. The email included three options in order to enable the advisory board to go ahead. The Appeal Board noted AstraZeneca agreed that the email of 8 November 2017 was poorly worded. The email referred to ensuring the company did not attract an audit and mentioned a self-report to the ABPI if the meeting went ahead as planned. The Appeal Board noted the submission from AstraZeneca that the senior UK medical department employee was new and that the self-report was in relation to the breach of the company's SOPs and not in relation to the ABPI Code. The Appeal Board considered that the reference to self-report appeared to be in relation to the Code. The Appeal Board noted that the email of 8 November 2017 had been copied to several senior AstraZeneca members of staff including some who represented the company at the Appeal Board meeting. The Appeal Board queried why nobody had replied to the email to raise their concerns. AstraZeneca stated that there had been a discussion about the email at the time but there was no written record. Although there was no requirement to self-report, the Appeal Board queried why the company had not self-reported a breach of Clause 14.2 at this point. AstraZeneca stated that this had been an oversight by the company.

The Appeal Board considered that when submitting a response, companies need not include everything however the company had not provided the relevant source material it used in summarising events. The email of 8 November 2017 was clearly central and relevant to this case and did not appear to be consistent with the summary provided. In the Appeal Board's view to not submit the email was inexplicable. Effective self-regulation required companies to be open and transparent when responding to complaints; they had a duty to disclose all relevant documents and information. When compiling its response to the complaint the representatives from AstraZeneca stated that they had referred to emails. The Appeal Board was not satisfied with AstraZeneca's submission as to why it had not provided the email dated 8 November when responding to the complaint.

The Appeal Board considered that the email of 8 November 2017 was clearly relevant and

should have been provided to the PMCPA as part of AstraZeneca's response. Notwithstanding AstraZeneca's submission that it now had updated its processes, the Appeal Board noted that self-regulation relied, *inter alia*, upon the provision of complete and accurate information from pharmaceutical companies. The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, AstraZeneca should be publicly reprimanded for failing to provide complete and accurate information in an open and transparent way.

The Appeal Board was concerned to note that AstraZeneca was also publicly reprimanded in 2016 by the Appeal Board for providing inaccurate information to the Panel (Case AUTH/2793/9/15).

The Appeal Board noted the Panel's comments above regarding AstraZeneca's conduct in responding to complaints. The Appeal Board noted its concerns about AstraZeneca's compliance culture. The Appeal Board gave consideration to the imposition of further sanctions including whether an audit should be required. However, on balance, the Appeal Board decided that no additional action was required.

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| **Complaint received** | **22 January 2018** |
| **Undertaking received** | **10 April 2018** |
| **Panel reconvened** | **2 May 2019** |
| **Appeal Board consideration** | **11 July 2019** |
| **Case completed** | **11 July 2019** |
| **Updated case report Including addendum published** | **3 February 2020** |

**CASE AUTH/3027/3/18**

# VOLUNTARY ADMISSION BY SUNOVION

## Disclosure of funding to a patient organisation and provision of inaccurate information

**Sunovion Pharmaceuticals Europe voluntarily admitted a breach of the Code in relation to its failure to disclose support to patient organisations as required by the Code and the provision of inaccurate information to the PMCPA.**

**As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Sunovion.**

**Sunovion admitted that in its comments on the PMCPA audit report in relation to Case AUTH/2935/2/17 it had stated that it had not worked with any patient organisations. However, the company regretted that it had now found this not to be so. In 2016, Sunovion entered in to an agreement with a registered charity supporting patients with mental health problems. In September 2016 and June 2017 Sunovion paid the patient organisation to support administration and general running costs. In addition, Sunovion paid for the development of an early intervention guide for patients with schizophrenia and their families. Part of this was paid in October 2016 and the remaining amount in February 2017. The support provided was declared on the company's website from 15 March 2018.**

**The detailed response from Sunovion is given below.**

**The Panel noted that the Code required, *inter alia*, that each company must make publicly available, at a national or European level, a list of patient organisations to which it provided financial support and/or significant indirect/non-financial support, which must include a description of the nature of the support that was sufficiently complete to enable the average reader to form an understanding of the significance of the support. The list of organisations being given support must be updated at least once a year. The relevant supplementary information stated that companies were encouraged to be prepared to make available up-to-date information about such activities at any time in response to enquiries.**

**The Panel acknowledged that it was not entirely clear whether as a minimum companies could update their lists on a certain date once a year covering the previous twelve months of payments in which case no payment would ever be disclosed more than twelve months after it was made or whether the annual update could be by no later than the 31 March each year in relation to payments made in the previous calendar year. This latter approach would be consistent with the relevant supplementary information in the 2012 edition of the Code and similar to the permitted approach when disclosing transfers of value under the Code. The Panel noted that as a minimum the published list of patient organisations had to be updated annually.**

**The Panel considered that the approach adopted by a company should be made clear on its website. Sunovion made no submission in this regard. The Panel considered it prudent and good practice for a company to update its list as soon as reasonably possible and noted that the relevant Clause referred to updating the list at least once a year.**

**The Panel noted that Sunovion had paid a patient organisation in October 2016 to support administration and general running costs. A copy of the certified agreement covering the payment in 2016 was provided. The agreement also covered payments in 2017 and 2018, but neither of these payments had been made contrary to the company's disclosure on 15 March 2018. That disclosure was updated on 27 March.**

**The Panel noted that in addition Sunovion had paid for the development of an early intervention guide for patients; part of this was paid in October 2016 and the remaining amount was paid in February 2017. The Panel noted Sunovion's submission that there was no written agreement to cover this payment and that the amount of support was less than that originally thought and disclosed on 15 March 2018 and was therefore updated on 27 March 2018.**

**The Panel noted the ambiguity of the Clause which covered disclosure of payments to patient organisations as described above but considered that regardless of the approach taken the two 2016 payments had not been disclosed as required by the Code and a breach of the Code was ruled in relation to both 2016 payments.**

**The Panel noted that the incorrect February 2017 payment was disclosed by 15 March 2018 and updated on 27 March 2018 to accurately reflect the amount actually paid. The Panel noted the ambiguity of the relevant Clause and considered on balance that disclosure prior to 31 March the following calendar year was not unacceptable and ruled no breach of the Code in relation to the 2017 payment.**

**The Panel noted the sensitivities surrounding the pharmaceutical industry working with patient organisations; robust agreements setting out the arrangements, and certification of those agreements were important steps in ensuring that such interactions complied with the Code and in that regard they underpinned the self-regulatory compliance system. That projects and sponsorship were able to go ahead without a certified agreement in place was unacceptable. Further, public disclosure of support was an important means of building and maintaining confidence in the industry.**

**The Panel noted that Sunovion had sponsored the development of an early intervention guide without first having a certified agreement in place and the company's support for the patient organisation in 2016, was not properly disclosed until March 2018. Whilst a certified agreement was in place for the separate payment to the patient organisation in 2016 overall the Panel considered that high standards had not been maintained. A breach of the Code was ruled.**

**The Panel was further concerned that the information provided in response to the PMCPA's audit report was incorrect and further that only in response to the case preparation manager's request for further comments, did Sunovion discover that the amount of financial support paid was less than stated in its initial voluntary admission. This, coupled with the fact that there was no certified agreement for one payment, in the Panel's view, indicated that there was poor governance and control of materials. The Panel noted that self-regulation relied, *inter alia*, upon the provision of complete and accurate information and that Sunovion had already been criticised for not providing accurate information in the case that led to the company being audited, Case AUTH/2935/2/17. The Panel considered that Sunovion had brought discredit upon or reduced confidence in the industry and therefore the Panel ruled a breach of Clause 2.**

**Sunovion provided the requisite undertaking and assurance and the Appeal Board received the case report as set out in Paragraph 13.4 of the Constitution and Procedure.**

**The Appeal Board noted the Panel's rulings of breaches of the Code regarding the voluntary admission from Sunovion about disclosure of payments made to patient organisations. The Panel had considered it was a serious matter.**

**The Panel's concerns included that the information provided in response to the PMCPA's audit report in another case concerning Sunovion, Case AUTH/2935/5/17 was incorrect. Further only in response to the case preparation manager's request for further comments in Case AUTH/3027/3/18 did Sunovion discover that the amount of financial support paid was less than stated in its initial voluntary admission. This coupled with the fact that there was no certified agreement for the payment of £2,750 in the Panel's view indicated that there was poor governance and control of materials. The Panel noted that self-regulation relied, *inter alia*, upon the provision of complete and accurate information and that Sunovion had already been criticised for not providing accurate information in Case AUTH/2935/2/17.**

**The Appeal Board considered that Case AUTH/3027/3/18 raised serious issues including about the provision of incomplete and/or inaccurate information. The Appeal Board was of the view that consideration should be given to imposing further sanctions under Paragraph 11.1 of the Constitution and Procedure.**

**The company was advised that the Appeal Board was considering imposing additional sanctions and asked to respond in writing, as well as be given the opportunity to appear before the Appeal Board when the matter was considered. Sunovion was provided with a copy of the papers.**

**The detailed comments from Sunovion about the possible imposition of further sanctions is given below.**

**The Appeal Board noted that the company had apologised and admitted that it had made errors.**

**The Appeal Board was concerned that due to poor judgement and/or absence of the necessary process the company had made a series of errors about its disclosure of payments in its responses to the PMCPA including during the re-audit required in Case AUTH/2935/2/17 in which it had already been criticised for not providing accurate information. Notwithstanding Sunovion's submission that it now had a process in place to ensure such errors did not recur, the Appeal Board noted that self regulation relied, *inter alia*, upon the provision of complete and accurate information from pharmaceutical companies.**

**The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, Sunovion should be publicly reprimanded for providing inaccurate information to the PMCPA. Following consideration of the re-audit report and Sunovion's comments on it the Appeal Board's decision to require a further re-audit in Case AUTH/2935/2/17, the Appeal Board decided that the issues that had arisen in Case AUTH/3027/3/18 should the subject of an audit which would take place April 2019 at the same time as the re-audit in Case AUTH/2935/2/17. On receipt of the report of the audit the Appeal Board would consider whether further sanctions were necessary.**

**Sunovion was audited in April 2019 and on receipt of the report of the audit in July 2019 the Appeal Board noted that there had been significant progress at Sunovion since the re-audit in June 2018 in Case AUTH/2935/5/17. The Appeal Board noted that Sunovion had a compliance action plan to address recommendations from the re-audit. The Appeal Board noted some actions were already completed and that others were due to be completed very shortly. On the basis that this work was completed, the progress shown to date was continued and a company-wide commitment to compliance was maintained, the Appeal Board decided that no further action was required.**

Sunovion Pharmaceuticals Europe Ltd voluntarily admitted a breach of the Code as it had not disclosed support it had given to a patient organisation.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Sunovion.

**VOLUNTARY ADMISSION**

In its voluntary admission Sunovion stated that in its comments on the PMCPA audit report in relation to Case AUTH/2935/2/17 it had stated that it had not worked with any patient organisations. However, the company regretted that it had now found this not to be so. In 2016, Sunovion entered in to an agreement with a registered charity supporting patients with mental health problems. In September 2016 and June 2017 Sunovion paid the patient organisation £10,000 to support administration and general running costs. In addition, Sunovion paid £4,900 for the development of an early intervention guide for patients with schizophrenia and their families. £600 of this was paid in October 2016 and the remaining £4,300 was paid in February 2017. The support provided was declared on the company's website from 15 March, 2018.

To prevent this happening in the future, the company introduced a standard operating procedure (SOP) covering work with patient organisations as part of its SOP action plan. It would ensure that all personnel who might become involved with patient organisations were trained on this. Sunovion would not initiate new activities with patient organisations until this was in place.

The company apologised unreservedly for providing inaccurate information in response to the audit report and accepted that Sunovion had breached Clause 27.7 by failing to publicly declare this support in good time.

Sunovion was asked to respond to Clauses 9.1 and 2 in addition to Clause 27.7.

**RESPONSE**

Sunovion stated that it had investigated the payments to the patient organisation and confirmed that the following payments were made. The amount of financial support was less than originally thought. In October 2016, £10,000 was provided. In addition, £600 was provided in October 2016 to support the development of an early intervention guide for patients, and a further £2,150 was provided in February 2017. A copy of the certified agreement covering the payment of £10,000 in 2016 was provided. The agreement also covered payments of £10,000 in 2017 and 2018, but these payments had not yet been made. Sunovion had searched its records and could not locate an agreement covering the £2,750 for the development of an early intervention guide. It appeared that an agreement was not put in place.

Sunovion submitted that the following appeared on its website:

> 'We believe in working transparently with the patient organisations that we engage with. In October 2016 we paid [a patient organisation] £10,000 to support administration and general running costs. In addition, we paid £2,750 for the development of an early intervention guide for patients. £600 of this was paid in October 2016 and the remaining £2,150 was paid in Feb 2017….'

The initial disclosure went live on 15 March 2018, and the information was amended as above on 27 March.

In addition to a breach of Clause 27.7, Sunovion stated that it had also breached Clause 27.3 by failing to have an agreement in place covering all work with the patient organisation in this case. It was with regret that Sunovion acknowledged that high standards had not been maintained and accepted that a breach of Clause 9.1 had occurred. Sunovion submitted that the matter did not bring discredit upon, or reduce confidence in, the industry and therefore a breach of Clause 2 had not occurred.

**PANEL RULING**

The Panel noted that Clause 27.7 stated, *inter alia*, that each company must make publicly available, at a national or European level, a list of patient organisations to which it provided financial support and/or significant indirect/non-financial support, which must include a description of the nature of the support that was sufficiently complete to enable the average reader to form an understanding of the significance of the support. The list of organisations being given support must be updated at least once a year. The relevant supplementary information stated that companies were encouraged to be prepared to make available up-to-date information about such activities at any time in response to enquiries.

The Panel acknowledged that it was not entirely clear whether as a minimum companies could update their lists on a certain date once a year covering the previous twelve months of payments in which case no payment would ever be disclosed more than twelve months after it was made or whether the annual update could be by no later than the 31 March each year in relation to payments made in the previous calendar year as set out in previous versions of the Code. This latter approach would be consistent with the relevant supplementary information in the 2012 second edition of the Code and similar to the permitted approach when discussing transfers of value under Clause 24.4. The Panel noted that as a minimum the published list of patient organisations had to be updated annually.

The Panel considered that the approach adopted by a company should be made clear on its website. Sunovion made no submission in this regard. The Panel considered it prudent and good practice for a company to update its list as soon as reasonably possible and noted that the Clause referred to updating the list **at least** once a year.

The Panel noted that Sunovion had paid a patient organisation, £10,000 in October 2016 to support administration and general running costs. A copy of the certified agreement covering the payment of £10,000 in 2016 was provided. The agreement also covered payments of £10,000 in 2017 and 2018, but neither of these payments had been made yet contrary to the company's disclosure on 15 March 2018. The disclosure was updated on 27 March.

The Panel noted that in addition Sunovion had paid £2,750 for the development of an early intervention

guide for patients; £600 of this was paid in October 2016 and the remaining £2,150 was paid in February 2017. The Panel noted Sunovion's submission that there was no written agreement to cover this payment and that the amount of support was less than that originally thought and disclosed on 15 March 2018 and was therefore updated on 27 March 2018.

The Panel noted the ambiguity of Clause 27.7 as described above but considered that regardless of the approach taken the two 2016 payments had not been disclosed as required by Clause 27.7 and a breach of that Clause was ruled in relation to both 2016 payments.

The Panel noted that the incorrect February 2017 payment of £4300 was disclosed by 15 March 2018 and updated on 27 March 2018 to accurately reflect the amount of £2150 actually paid. The Panel noted the ambiguity of Clause 27.7 and considered on balance that disclosure prior to 31 March the following calendar year was not unacceptable and ruled no breach of this clause in relation to the 2017 payment.

In its response Sunovion raised Clause 27.3 of the Code which required that companies working with patient organisations have a written agreement in place which set out exactly what had been agreed, including funding, in relation to every significant activity or on-going relationship. Clause 14.3 required such agreements to be certified in advance. The Panel could make no ruling under this clause as it had not been raised in Sunovion's initial voluntary admission nor had Sunovion been asked to respond to it. Whilst not the subject of the voluntary admission *per se* it was nonetheless relevant to the matters before the Panel.

The Panel noted the sensitivities surrounding the pharmaceutical industry working with patient organisations; robust agreements setting out the arrangements, and certification of those agreements were important steps in ensuring that such interactions complied with the Code and in that regard they underpinned the self-regulatory compliance system. That projects and sponsorship were able to go ahead without a certified agreement in place was unacceptable. Further, public disclosure of support was an important means of building and maintaining confidence in the industry. The Panel noted that Sunovion had sponsored the development of an early intervention guide without first having a certified agreement in place and the company's support for the patient organisation in 2016, was not properly disclosed until March 2018. Whilst a certified agreement was in place for the separate payment of £10,000 to the patient organisation in 2016 overall the Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel was further concerned that the information provided in response to the PMCPA's audit report was incorrect and further that only in response to the case preparation manager's request for further comments, did Sunovion discover that the amount of financial support paid was less than stated in its initial voluntary admission. This, coupled with the fact that there was no certified agreement for the payment of £2,750, in the Panel's view, indicated that there was poor governance and control of materials. The Panel noted that self-regulation relied, *inter alia*, upon the provision of complete and accurate information and that Sunovion had already been criticised for not providing accurate information in the case that let to the company being audited, Case AUTH/2935/2/17. The Panel considered that Sunovion had brought discredit upon or reduced confidence in the industry and therefore the Panel ruled a breach of Clause 2.

**APPEAL BOARD CONSIDERATION OF CASE REPORT**

Sunovion provided the requisite undertaking and assurance and as the case completed at Panel level the Appeal Board was provided with certain papers (the Panel minute and the case report) as was usual for such cases (Paragraph 4.1 of the Constitution and Procedure).

The Appeal Board noted the Panel's rulings of breaches of Clauses 2, 9.1 and 27.7 regarding the voluntary admission from Sunovion about disclosure of payments made to patient organisations. The Panel had considered it was a serious matter.

The Panel's concerns included that the information provided in response to the PMCPA's audit report in another case concerning Sunovion, Case AUTH/2935/2/17 was incorrect. Further only in response to the case preparation manager's request for further comments in Case AUTH/3027/3/18 did Sunovion discover that the amount of financial support paid was less than stated in its initial voluntary admission. This coupled with the fact that there was no certified agreement for the payment of £2,750 in the Panel's view indicated that there was poor governance and control of materials. The Panel was further concerned that the information provided in response to the PMCPA's audit report was incorrect. The Panel noted that self-regulation relied, *inter alia*, upon the provision of complete and accurate information and that Sunovion had already been criticised for not providing accurate information in Case AUTH/2935/2/17.

The Appeal Board considered that Case AUTH/3027/3/18 raised serious issues including about the provision of incomplete and/or inaccurate information. The Appeal Board was of the view that consideration should be given to imposing further sanctions under Paragraph 11.1 of the Constitution and Procedure.

The company was advised that the Appeal Board was considering imposing additional sanctions and asked to respond in writing, as well as be given the opportunity to attend the next meeting of the Appeal Board when the matter would be considered. Sunovion was provided with a copy of the papers.

**COMMENTS FROM SUNOVION**

Sunovion submitted that it understood and accepted the serious nature of the concerns the Appeal

Board had in relation to this case as well as Case AUTH/2935/2/17. Sunovion apologised unreservedly for providing inaccurate and incomplete responses to these cases and to the PMCPA's audit report.

Sunovion summarised the background to these events, in 2016, a Sunovion employee (no longer with the company) commenced relations with a patient organisation, a registered charity supporting patients with mental health problems. In September 2016, a certified agreement was put in place to pay the patient organisation £10,000 per annum over a period of three years to support its administration and general running costs. Payments for this purpose were made in October 2016 for the fiscal year 2016 payment, April 2018 for the fiscal year 2017 payment and July 2018 for the fiscal year 2018 payment. The support Sunovion provided was declared on its website from 15 March 2018. This declaration reflected the scheduled payment dates as set out in the certified agreement with the patient organisation rather than the actual dates of payments which subsequently ensued. Additionally, as identified during the PMCPA re-audit on 30 June 2018, the initial payment of £10,000 in October 2016 was included in the company's submission to Disclosure UK for 2016, as a payment to a healthcare organisation; this was subsequently removed and the support disclosed on Sunovion's website as a patient organisation payment. Sunovion acknowledged and regretted these errors and to prevent future occurrences it would ensure that payment details, including dates were checked against the finance payment system rather than the agreement payment schedule.

In addition, the same employee arranged for Sunovion to financially support the patient organisation to produce an early intervention guide for patients with schizophrenia and their families. To this end, £600 was paid in October 2016 and the remaining £2,150 was paid in February 2017. Sunovion had not been able to locate an agreement covering the development of this guide, indicating that one was not in place. This support was disclosed on Sunovion's website from 15 March 2018 and updated on 27 March 2018 when the original figure disclosed ie £4,300 was found to be incorrect; the figure was amended to £2,150. This was due to an incorrect reading of data from the company's finance system. In future, all such figures would be double checked by a member of the finance team before public declarations were made. Again, Sunovion acknowledged and regretted this error.

In preparation for the PMCPA audit in Case AUTH/2935/2/17 in June 2018, Sunovion noted that it was asked to produce all papers in relation to disclosures of transfers of value on Disclosure UK (2016 data disclosed in 2017) for: a patient organisation, £103.98. Prior to the day of the audit following the PMCPA document request, Sunovion became aware that two copies of prescribing guidelines were provided to a patient organisation in March 2016. The total value of the books was £103.98. On discovering this, Sunovion engaged an independent expert to re-audit its records. Two further incidents were found:

- A meeting was organised by Sunovion in December 2015 involving four members of patient organisations. A grant of £187.10 was provided to support one patient organisation, and a grant of £192 was provided to another patient organisation to cover travel and accommodation. This support was covered by a certified agreement signed by the patient organisation and Sunovion Pharmaceuticals Europe in both cases.

- A further copy of prescribing guidelines was supplied to a patient organisation in 2016, with a value of £51.99.

Sunovion submitted that all were disclosed as transfers of value to a healthcare organisation or a health professional. The support for a patient organisation, was disclosed on Disclosure UK in 2016 as part of Sunovion's 2015 disclosures, and the support for another two patient organisations were disclosed in 2017 as part of Sunovion Pharmaceuticals Europe's 2016 disclosures. The support for one patient organisation was treated as a transfer of value to a health professional. The individual declined consent to disclose and this was disclosed in aggregate as part of Sunovion Pharmaceuticals Europe's 2015 disclosures in 2016. However, the individual was not a health professional. It was clear that these should all have been processed and disclosed as financial and indirect/non-financial support to a patient organisation under Clause 27.7. As the Authority would be aware, these irregularities were identified on the day of the PMCPA audit and Sunovion expressed its regret at this time.

Sunovion submitted that these payments were disclosed on its website on 9 July 2018, and the entries removed from Disclosure UK by 13 July 2018. Details of the statement on Sunovion's website of declaration of Sunovion's involvement with patient organisations were provided.

Sunovion submitted that to prevent this happening in the future a new policy had been written to encompass all interactions with patient organisations. Every member of Sunovion staff had received face-to-face training, as well as passed a validation on this policy. In addition, working with patient organisations had been incorporated into the Annual Monitoring Plan. The monitoring activities would include six monthly checks within the electronic approval system, checks within the financial systems as well as annual checks on Sunovion's transfer of value declaration prior to its submission to the Disclosure UK portal to ensure accurate disclosures.

Sunovion deeply regretted the events that had led to this case. As an organisation, Sunovion submitted that it was committed to developing a strong and robust compliance culture and that it was making considerable progress in this direction, whilst acknowledging that it still had some way to go.

In relation to the possibility of further sanctions, Sunovion submitted that the original issues did not reflect current company practice and indeed

the individual involved had left the organisation some time ago. The recent mistakes in disclosures, identified during responding to the PMCPA and the preparation for audit, had been acknowledged and the company proposed actions to prevent recurrence. Although at the time of the response in Case AUTH/3027/3/18 Sunovion had not yet received the PMCPA's report following the re-audit in June, Sunovion anticipated that this would demonstrate the progress made recently in establishing and embedding compliance systems and culture within its organisation. Sunovion accepted the jurisdiction of the Appeal Board and its authority to impose further sanctions but anticipated that these be considered in context, particularly the re-audit report.

At the consideration of this matter the Sunovion representatives presented an outline of the company's commitment to a compliant culture, a brief summary of Case AUTH/2935/2/17 and Case AUTH/3027/3/18 and noted key changes since the November 2017 audit. Sunovion's representatives also apologised unreservedly for its failings and stated that the company acknowledged and regretted these errors and to prevent future occurrences it would ensure that figures would be checked by the finance team before public declarations were made. A new policy and standard operating procedure would ensure that payments were disclosed correctly.

**APPEAL BOARD CONSIDERATION**

The Appeal Board noted the Panel's rulings of breaches of Clauses 2, 9.1 and 27.7 of the Code. The Appeal Board noted that the company had apologised and admitted that it had made errors.

The Appeal Board was concerned that due to poor judgement and/or absence of the necessary process the company had made a series of errors about its disclosure of payments in its responses to the PMCPA including during the re-audit required in Case AUTH/2935/2/17 in which it had already been criticised for not providing accurate information. Notwithstanding Sunovion's submission that it now had a process in place to ensure such errors did not recur, the Appeal Board noted that self regulation relied, *inter alia*, upon the provision of complete and accurate information from pharmaceutical companies.

The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, Sunovion should be publicly reprimanded for providing inaccurate information to the PMCPA.

Following consideration of the re-audit report and Sunovion's comments on it and the Appeal Board's decision to require a further re-audit in Case AUTH/2935/2/17, the Appeal Board decided that Case AUTH/3027/3/18 should the subject of an audit which would take place April 2019 at the same time as the re-audit in Case AUTH/2935/2/17. On receipt of the report of the audit/re-audit the Appeal Board would consider whether further sanctions were necessary.

**APPEAL BOARD FURTHER CONSIDERATION**

Sunovion was audited in April 2019 and on receipt of the report of the audit in July 2019 the Appeal Board noted that Sunovion Pharmaceuticals Europe had continued to build on the improvements described in the report of the June 2018 re-audit in Case AUTH/2935/5/17. Staff had spoken positively about the steps taken by Sunovion Pharmaceuticals Europe to improve its compliance infrastructure. Compliance was now the top priority for the global Japanese parent, Sumitomo Dainippon. Sunovion Pharmaceuticals Inc in the US accepted that Sunovion Pharmaceuticals Europe was the subject matter expert on the Code. It was noted that the general manager continued to give strong and consistent messages about the importance of compliance and that compliance was now part of everybody's objectives.

The Appeal Board noted that the re-audit report still highlighted concerns including with regard to updating standard operating procedures and policies.

The Appeal Board noted that there had been significant progress at Sunovion since the re-audit in June 2018. The Appeal Board noted that Sunovion had a compliance action plan to address recommendations from the re-audit. The Appeal Board noted some actions were already completed and that others were due to be completed very shortly. On the basis that this work was completed, the progress shown to date was continued and a company-wide commitment to compliance was maintained, the Appeal Board decided that no further action was required.

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|---|---|
| **Voluntary admission received** | **16 March 2018** |
| **Undertaking received** | **26 June 2018** |
| **Appeal Board consideration** | **13 September 2018, 11 July 2019** |
| **Interim case report first published** | **30 November 2018** |
| **Case completed** | **11 July 2019** |

**CASE AUTH/3031/4/18**

# ANONYMOUS NON-CONTACTABLE HEALTH PROFESSIONAL v GILEAD

## Speaker training meeting

**An anonymous, non-contactable health professional alleged that a Gilead Oncology Faculty Meeting held in Frankfurt in March 2018, constituted disguised promotion of Zydelig (idelalisib). Zydelig was used in certain adult patients with either chronic lymphocytic leukaemia (CLL) or follicular lymphoma (FL).**

**The complainant stated that it was only after arriving that he/she found out that the premise of the meeting was to train speakers on Zydelig and for them then to go out and speak about the medicine. This was not made entirely clear beforehand. The complainant submitted that the content was not balanced medical education.**

**Throughout the meeting Zydelig was shown in a positive light and competitors in a negative light. The meeting revolved around Zydelig – there was no balance. Even in a statistics lecture, the worked examples were chosen to cast doubt on either competitor data, or data which could be perceived as negative for Zydelig. The complainant alleged that this disparaged competitor medicines and was clearly promotional in tone and content.**

**The complainant alleged that the meeting co-chair from Gilead was overtly biased in that he/she actively took part in discussions and directed the meeting in a way that one would have expected at a promotional meeting. The co-chair brought up positive aspects of Zydelig and disparaged one competitor medicine and questioned the validity of data on another. Further, he/she asked questions of the speakers so that positive Zydelig data would be discussed, even off-label data.**

**The complainant stated that on day 2 he/she was appalled to hear Zydelig positioned as a preventative treatment for Richter's transformation (RT) in chronic lymphocytic leukemia. There was no data to support those claims; it was all hypothesis and postulation.**

**Gilead appeared to accept and verbalize these hypotheses that Zydelig was an 'immuno-oncology compound which suppressed the high-risk clones' as fact, without any data to support the claims. A table used to highlight a lower rate of RT with Zydelig used data from off-label studies – this slide was freely available for delegates to download afterwards from the Gilead Oncology Faculty Portal. The complainant alleged that there was off-label data throughout the portal (which consisted of hundreds of slides).**

**The complainant also noted that half of the attendees were from Italy. The complainant queried whether they all went out and talked about Zydelig following the meeting, or even a substantial proportion of them. The meeting appeared to be a reasonably efficient way for Gilead to have a large contingent held captive for two days while paid speakers promoted to them.**

**The detailed response from Gilead is given below.**

**The Panel noted Gilead's explanation that the Gilead Oncology Faculty was a register of trained speakers but it queried whether the title of the meeting, Gilead Oncology Faculty meeting, fairly reflected the stated purpose of the meeting. In the Panel's view such faculties were often used to describe company convened meetings of key opinion leaders and such like. The impression given by the title of the meeting was important.**

**The Panel noted Gilead's submission that the meeting was an appropriate training meeting to ensure that health professionals whom the company intended to engage to speak on its behalf had a detailed understanding of the clinical dataset. When determining whether the content was appropriate the Panel considered that the overall arrangements, the therapy area and the professional status of the delegates were relevant. In the Panel's view, delegates should know at the outset and before their attendance that the meeting was a speaker training event and that they would be engaged as speakers thereafter.**

**The Panel noted that speaker contracts were covered by contracts with consultants. The Panel considered that in principle it was good practice when training speakers to fulfil future speaker engagements to ensure that a written agreement covered the training activity to ensure that the arrangements including the nature of the meeting, the context in which data was presented and the parties' responsibilities and relationship were clear. Such written agreements were particularly important if the material disseminated referred to off-licence data so that the context of such references was clear. The Panel noted that there was a difference between interacting with a health professional as a prescriber and interacting with him/her as a consultant. Interactions with a health professional in his/her capacity other than as a prescriber, eg speaker training, might be considered non-promotional. In such circumstances, and where directly relevant, the provision of relevant unlicensed data to the health professional might not be contrary to the Code which prohibited the promotion of unlicensed data or data that was inconsistent with the terms of a product's marketing authorisation. The provision of such data to individuals who were training to be speakers should comply with the Code.**

**In relation to the meeting in question the Panel noted that no monies were paid to delegates who were not also presenting. The Panel noted that the contract for UK delegates was headed 'Support for individual attendance at an event' and did not refer to a training event; it appeared, in the Panel's view, akin to a contract for sponsorship to attend a clinical meeting as a delegate. The Panel noted its comments above about the impression given by the title of the meeting.**

**The Panel noted that the health professionals who attended and who were existing members of the faculty and who, unless presenting at the meeting in question, were invited for the second day and had the option to also attend on day one; new members to the faculty were invited to attend both days.**

**The Panel queried whether the purpose of the meeting was sufficiently clear at the outset to all invitees, particularly new faculty members. In the Panel's view the emails were not sufficiently clear that the primary purpose of the meeting in question was to train speakers and that the clinical data was presented for that purpose, rather the emails implied that it was an invitation to attend a meeting about oncology therapy and idelalisib, part of which would include presentation skills training. Whilst some details about the presentation skills sessions were given in the detailed agenda, the agenda still appeared primarily to describe a clinical meeting and did not negate the otherwise misleading impression about the primary purpose of the meeting given by the invitation emails. The reference to the faculty programme in the invitation and agenda implied that there was an ongoing clinical programme.**

**The Panel noted Gilead's submission about the selection criteria. The Panel did not know when the UK delegates had first been contacted to attend the meeting but noted that an email dated 26 July 2017 from the European company asked affiliates to nominate local health professionals and implied that the primary purpose of the meeting in question was to enable delegates to acquire in-depth clinical knowledge, including about idelalisib. Although the email dated 26 July referred to training and speakers, the Panel considered that overall this was not given sufficient prominence; training was presented as just one of several benefits of the meeting. In addition the rationale for selection subsequently given by the UK affiliate to the European company did not refer to the potential delegates' suitability as speakers and the company's intention to engage them as such. Although the UK company subsequently confirmed to the European company that 'the plan is to engage the HCP', there was no evidence before the Panel that UK health professionals had been so informed.**

**The Panel noted Gilead's submission that the purpose of the meeting and expectations of delegates after the meeting were clearly communicated at the meeting itself, this was too late. The Panel considered that the failure to make the intended purpose of the meeting sufficiently clear at the outset meant that high standards had not been maintained. A breach of the Code was ruled. The Panel noted its comments above about the impression given by the arrangements and considered that invitees would, on the balance of probabilities, consider that they were being invited to a promotional meeting and in this regard the Panel did not consider that the meeting was a disguised promotional activity. No breach of the Code was ruled.**

**The Panel noted the complainant's allegation that the meeting was not balanced education and that promotional techniques were used throughout. The complainant stated that examples were chosen of idelalisib in a positive light and competitors in a negative light and had referred, in particular, to a statistics presentation. The Panel noted the complainant bore the burden of proof and had not explained why the particular worked examples were disparaging; he/she had not provided sufficient detail to establish why the presentation in question was disparaging or unbalanced. No breach of the Code was ruled.**

**The Panel noted that the complainant alleged that the co-chair was biased and had, in particular, referred to the increased risk of infection associated with a competitor. Gilead submitted that the latter comment was a statement of fact and referred to the infections listed as common in the relevant SPC. It was not clear precisely what had been said by the co-chair although it was clear that he/she had commented on the subject matter of the complaint. The Panel also noted Gilead's submission that the comments were made in response to an unsolicited question. Noting that the complainant bore the burden of proof, and Section 4.8 of the competitor SPC, the Panel considered that it had not been established that comments by the co-chair about the competitor were unbalanced. No breach of the Code was ruled on this point.**

**In relation to an allegation that the co-chair was biased as he/she questioned the validity of data on another competitor, the Panel noted Gilead's submission that it had no recollection of the co-chair making such a statement and that this was reflected in the meeting summary. The Panel noted that the responses in the meeting summary did not appear to question the validity of the competitor data as alleged. The complainant bore the burden of proof. The Panel considered that it had not been established that the validity of the data had been questioned as alleged. No breach of the Code was ruled.**

**The Panel noted the allegation that the Gilead co-chair deliberately asked questions of speakers so that positive idelalisib data would be discussed, including off-label data. The Panel considered that given the product and therapy area, speakers might be asked questions about unlicensed data and it was not unreasonable to train them to address such questions so long as, overall, the activity otherwise complied with the Code. The Panel noted that the complainant bore the burden of proof. The Panel noted its concerns above but, on balance, considered that there was insufficient evidence before it and no breach was ruled.**

**The Panel noted the allegation that idelalisib was being positioned as a preventative treatment for**

**Richter's transformation in CLL and that there was no data to support these claims. The Panel noted idelalisib's licensed indication as part of the treatment of certain adult patients with CLL. The Panel noted its general comments above about the provision of data about the unlicensed use of a product as part of a formal speaker training event.**

**The Panel noted Gilead's submission that a presentation entitled 'Prevention of Richter's transformation' was provided to train participants on the clinical unmet need in patients with CLL who progress with Richter's transformation. Gilead also stated that the session was delivered to train participants to respond appropriately if asked about this topic when delivering presentations on idelalisib. The Panel considered that given the therapy area, in principle, it was not unreasonable, within the context of *bona fide* speaker training, to train participants to answer unsolicited questions about the off-licence use of a product.**

**The Panel noted that the presentation in question 'Prevention of Richter's transformation' was delivered on the afternoon of the final day. The summary slide described Richter's transformation as an unmet clinical need in CLL patients; the immediate preceding slide implied that Zydelig might satisfy that unmet clinical need. The Panel considered that other presentations also discussed idelalisib and Richter's transformation in positive terms. The Panel considered that the overall narrative of the presentations was such that they highlighted features of idelalisib, including its unique mechanism of action, in relation to the prevention of RT which was described in the final presentation as an unmet clinical need. The Panel considered that the presentations, together with the description of such comparative data as 'potentially practice changing' by a speaker who Gilead described as a globally respected expert and principal investigator was such that, on balance, the company positioned Zydelig as a preventative treatment for Richter's Transformation as alleged. A breach of the Code was ruled.**

**In relation to the allegation that Gilead accepted and verbalised the hypotheses about idelalisib being an 'immuno-oncology compound which supresses the high risk clones' without data to support such claims, the Panel noted Gilead's submission that it had no recollection or record of this being stated at the meeting. The Panel noted that the comment, or one closely similar, did not appear in the summary of Q&A. The Panel therefore considered that the complainant, who bore the burden of proof, had not established that the statement had been made and, on this basis, no breach of the Code was ruled.**

**In relation to the complainant's allegation about an imbalance of delegates from Italy, the Panel noted Gilead's explanation, including that the product was launched in Italy a few months before the safety signal emerged in March 2016 and Italian clinicians had little experience in managing adverse events at that time. The Panel did not consider that the proportion of Italian participants alone rendered the meeting inappropriate as a training event. No breach was ruled on this narrow point.**

An anonymous, non-contactable health professional complained about a Gilead Oncology Faculty Meeting held in Frankfurt in March 2018 which was described by Gilead as a speaker training meeting for Zydelig (idelalisib). Zydelig was used in certain adult patients with either chronic lymphocytic leukaemia (CLL) or follicular lymphoma (FL).

**COMPLAINT**

The complainant explained that he/she had been invited to attend a non-promotional Gilead Oncology Faculty Meeting which was organised and fully funded by Gilead.

The complainant stated that his/her main concern was that the meeting constituted disguised promotion. Despite being told on numerous occasions, verbally and on slides during the meeting, by the organisers that the meeting was non-promotional, he/she considered that Zydelig was promoted throughout the two days.

The complainant stated that it was only after arriving that he/she found out that the premise of the meeting was to train speakers on Zydelig and for them then to go out and speak about the medicine. Before the meeting, it was not made entirely clear that this would be the expectation following the meeting.

The complainant submitted that the content was not balanced medical education. Just because slides did not contain brand names/logos or overt promotional claims but did discuss safety/side effects did not make the meeting non-promotional. The complainant stated that he/she would expect that side effects were discussed during any interaction with a company representative. That was responsible promotion.

More subtle promotional tactics were used throughout the meeting eg Zydelig was shown in a positive light and competitors in a negative light. The meeting revolved around Zydelig. Even in a statistics lecture, the examples were chosen to cast doubt on either competitor data, or data which could be perceived as negative for Zydelig. The complainant alleged that this disparaged one competitor medicine in particular and was clearly promotional in tone and content.

The complainant alleged that the meeting co-chair from Gilead was overtly biased. At a non-promotional meeting, it would be expected that a company co-chair, would only move the meeting along in terms of timing/logistics and act as master of ceremonies. At the meeting in question, the co-chair actively took part in discussions, discussed data and actively directed the meeting in a way that the complainant would have expected at a promotional meeting. The co-chair brought up positive aspects of Zydelig and disparaged competitors with statements such as '[one medicine] has a lot of problems with infections' and questioned the validity of data on another which had recently been published in the

New England Journal of Medicine and which the complainant considered was so much better than the Zydelig data in CLL.

Furthermore, the Gilead co-chair deliberately questioned the speakers so that positive Zydelig data would be discussed, even off-label data. The co-chair proactively asked questions of speakers on favourable off-label Zydelig data eg a question on the RIALTO study – a frontline off-label combination of Zydelig. This was deliberately done to build a favourable image for Zydelig. The co-chair tried to get one of the speakers to state that after only 2.5 months of treatment with Zydelig there were long responses. The co-chair succeeded and a speaker spoke favourably about this study and potential long-term effects of Zydelig. The complainant noted that this discussion was based on off-label data, from a study which was stopped due to safety concerns, where a number of patients died due to Zydelig-related infections. This data was proactively referred to again on day two by another Gilead employee.

The complainant stated that on day two he/she was appalled to hear Zydelig positioned as a preventative treatment for Richter's transformation (RT) in CLL. There was no data to support those claims; it was all hypothesis and postulation. Tables showing different rates of RT with the different novel agents were shown and even the speaker said a number of times that any observed difference should be 'taken with a pinch of salt' due to differences between the studies and a number of other factors. The complainant submitted that cross-trial comparisons were risky and confounded.

Gilead appeared to accept and verbalize the hypotheses that Zydelig was an 'immuno- oncology compound which suppressed the high-risk clones as fact, without any data to support the claims. A table used to highlight a lower rate of RT with Zydelig used data from off-label studies – this slide was freely available for delegates to download afterwards from the Gilead Oncology Faculty Portal. The complainant alleged that there was off-label data throughout the portal (which consisted of hundreds of slides).

The complainant also noted the imbalance of attendees from certain countries – half were from Italy. The complainant queried whether they all went out and talked about Zydelig following the meeting, or even a substantial proportion of them. The complainant submitted that it appeared to be a reasonably efficient way for Gilead to have a large contingent held captive for two days while paid speakers promoted to them.

Overall, the complainant stated that a two day meeting discussing one product was wrongly classified as non-promotional; he/she objected strongly to the disguised promotion and constant disparaging of competitor molecules which were equally, or in most cases, more effective than Zydelig. The constant interference in the proceedings by an obviously biased Gilead employee, who proactively asked about off-label data, was unacceptable.

When writing to Gilead, the Authority asked it to respond to the requirements of Clauses 2, 3.2, 7.2, 7.3, 7.4, 8.1, 9.1, 11.1 and 12.1.

**RESPONSE**

Gilead explained that the meeting was organised by Gilead Sciences Europe Limited (GSEL), Gilead Science's headquarters for the Europe, Middle East and Australia (EMEA) region. GSEL was based in the UK.

Gilead did not consider that its arrangements for the meeting breached the Code. The meeting was an appropriate training meeting held to ensure that those health professionals whom GSEL intended to engage to speak on its behalf had a full and detailed understanding of the Zydelig data set. This meant that when they were engaged to present at Gilead-organised meetings they could present the data in a way that reflected the evidence for Zydelig in line with its marketing authorization.

Attendees were selected on clear and appropriate criteria and they were told about the nature and purpose of the meeting through the invitation process and again at the start of the meeting. The attendees were not paid for their attendance, unless they were specifically engaged to present during the meeting.

The meeting content consisted of appropriate and necessary education required to achieve the stated purpose. The content was accurate, balanced, fair, and could be substantiated. Any off-label information was clearly highlighted and only shared to ensure that participants fully understood the data set for Zydelig and could reflect the evidence for the medicine in line with its marketing authorization when engaged by Gilead. The attendees were trained on GSEL's requirements in relation to sharing any off-label data proactively, and how to appropriately handle any questions on off-label data.

**Background to the meeting and licensed indications for Zydelig in Europe**

The meeting was the Gilead Oncology Faculty meeting and was held to train the invited European health professionals on the latest clinical data and evidence related to Zydelig. The training was to prepare the delegates to speak about Zydelig on behalf of Gilead at company-organised meetings in countries within the region. GSEL had held a face-to-face Oncology Faculty training meeting once a year since 2015 (there were two held in 2015 when the Faculty was launched). A virtual meeting was also held in 2017.

Zydelig was indicated in Europe as follows:

> 'Zydelig is indicated in combination with an anti-CD20 monoclonal antibody (rituximab or ofatumumab) for the treatment of adult patients with chronic lymphocytic leukaemia (CLL):
> - who have received at least one prior therapy, or

- as first line treatment in the presence of 17p deletion or TP53 mutation in patients who are not eligible for any other therapies

Zydelig is indicated as monotherapy for the treatment of adult patients with follicular lymphoma (FL) that is refractory to two prior lines of treatment.'

On 10 March 2016, the European Commission (EC) was informed that an increased risk of death and a higher incidence of serious adverse events had been seen in Zydelig patients compared with the control groups in three Gilead sponsored clinical trials (NCT01980888, NCT01732913 and NCT01732926). The Pharmacovigilance Risk Assessment Committee (PRAC) subsequently assessed the risk/benefit of Zydelig in its licensed indications. The EC's final decision and assessment report resulted in the licensed indications as stated above.

The meeting provided the future speakers with accurate, balanced information about the safety and efficacy of Zydelig. The objective of the meeting was to ensure that they fully understood the data for Zydelig and its safety management to ensure they could present the data in a way that reflected the evidence for the medicine in line with its marketing authorization. Given the safety issues identified above, the complex safety profile of the medicine and the need for careful safety management of patients, the Faculty was a critical platform for ensuring patient safety.

**Delegate selection and participation**

GSEL maintained a register of trained speakers who could be engaged by Gilead country affiliates to speak about Zydelig - the Gilead Oncology Faculty ('the Faculty').

The meeting was held to train both new and existing members of the Faculty; it was structured as follows:

Day one was for new members to the Faculty and provided training, delivered by existing expert members of the Faculty, on the on-label Zydelig data. An agency delivered an interactive presentation skills training session about the importance of good presentation including preparation and presentation. Existing members of the Faculty who wanted to refresh their knowledge could opt in to day 1 if they wished.

Day two was for new and existing members of the Faculty and it provided training on new Zydelig on-label data (recent data from the preceding 12 months) and topics of relevance. Further interactive speaker skills training was provided.

The GSEL medical team worked with country affiliate medical teams to identify suitable potential new members to the Faculty. The potential new members invited to the meeting were selected based on their:

- ability to educate their peers about scientific information relating to Gilead's products and the diseases they treated;
- knowledge, expertise and skills to explain complex data and
- therapeutic experience required to respond appropriately to audience questions.

These criteria were communicated to delegates on day one of the meeting to provide further clarity on their role. In addition, the new Faculty members were selected on the basis that they:

- were already recognised as speakers or they wished to become speakers;
- expected to be engaged to speak at Gilead meetings;
- had a good professional standing within the haematology-oncology community;
- could speak engagingly in front of a larger group; and
- were likely to be available to take on additional speaker engagements.

As well as the new Faculty members, existing Faculty members were invited to the meeting provided they continued to meet the above criteria and provided the country affiliate teams continued to intend to engage them to speak on Gilead's behalf. Eight members of the Faculty were engaged to present at the meeting.

**What were the participants expected to do after the meeting?**

After the meeting delegates were expected to speak about the safety profile and efficacy of Zydelig, and its safety management at Gilead-organised events. The content for the meeting was focused on the topics that the delegates would be expected to present on in future events and to prepare them to appropriately answer questions from the audience. The meeting thus focused on Zydelig, with other approved agents mentioned where appropriate.

This expectation was highlighted in the invitations to the meeting and repeated on day one when the participants were briefed as to why they were selected and on Gilead's expectations and rules of engagement when they presented on Gilead's behalf.

**How many attended the meeting and were they paid? Participant list and their country of practice.**

GSEL provided a list of the 11 new and 11 existing Faculty members and the 8 external Faculty speakers who attended the meeting in addition to the 7 Gilead attendees. GSEL identified which days of the meeting they each attended and their countries of practice. There were 5 external participants from the UK - 3 Faculty speakers, 1 existing Faculty member and 1 new Faculty member. The meeting was facilitated by an external medical agency engaged by GSEL.

Faculty members who were engaged to present at the meeting were only paid for the time they spoke or participated as indicated on the agenda. The participants attending as new or existing Faculty members were not paid to attend the meeting but GSEL met their reasonable costs (or paid direct) for hospitality (travel, accommodation and subsistence) in accordance with GSEL's policy.

**How many of the participants had presented for Gilead at other meetings?**

All of the Faculty members engaged to present at the meeting had been engaged by Gilead and had delivered at least 59 presentations across the EMEA region since they became Faculty members. Gilead had engaged 4 of the other existing Faculty members attending the meeting to present on 14 occasions since they became Faculty members. The majority of these Faculty members first joined the Faculty in 2017.

Gilead maintained the Gilead Oncology Faculty so that it had a pool of speakers with an up-to-date knowledge of Zydelig who were able to speak on its behalf in a knowledgeable and compliant manner. Whether they were engaged to present could depend on many factors.

If a Faculty member had not been engaged to speak, this was a factor as to whether they were retained in the Faculty and invited to future training meetings, and this was monitored by the EMEA medical team. A lack of engagement would not necessarily mean they were removed from the Faculty and excluded from future training provided there was a continued intention to engage them (and there was an anticipated demand for meetings such that it was likely they would be engaged) and there was a good reason why future training to update their knowledge was considered necessary.

This was reviewed and discussed jointly by the EMEA and country medical teams. Given the detailed and technical product knowledge that speakers required, Gilead considered the Oncology Faculty meeting was an important training event for them, in particular for new or recently joined members.

**How many Gilead staff attended, how were they selected and their roles?**

Seven Gilead medical affairs staff from EMEA headquarters or from countries who nominated participants attended the meeting. No sales or marketing personnel attended. The selection of the medical team members was based on defined criteria.

A full list of the Gilead staff members who attended and their roles was provided.

**Code considerations**

With regard to the complainant's comments that the objective of the meeting (to train speakers on Zydelig) had not been made clear beforehand, GSEL explained that all participants, including those from UK, were informed in advance that the meeting was a training meeting as part of the Gilead Oncology Faculty programme. This was indicated on the email which invited the participants to register for the meeting and in the verbal discussion with the new participants inviting them to be members of the Gilead Oncology Faculty speakers programme.

The country teams had to speak to new Faculty members to explain to them the expectation that they would be asked to speak on behalf of Gilead at Gilead-organised events and to ensure that they were happy to be available to do this. The purpose of the meeting, and expectations after it, were again clearly communicated at the start and throughout the meeting, for example, in a presentation 'Your relationship with Gilead and participation in the Oncology Faculty' (copy provided). GSEL thus did not consider that the meeting was in breach of Clause 11.1 of the Code; it was reasonable to assume that all those attending were aware of the nature of the material they would receive and were happy to receive it. Gilead also denied a breach of Clause 12.1 as the meeting was a training meeting and not a promotional meeting and the purpose of the meeting was made clear to all attendees.

The content was driven by topics on Zydelig on which these speakers might speak proactively in future or be able to respond appropriately and compliantly to questions that audiences might ask. There was a focus on Zydelig, with other approved targeted agents also mentioned throughout the training where appropriate and relevant. There were substantial discussions on both days focused on adverse events and management of Zydelig; whole sessions were dedicated to on-label adverse event management and understanding the mechanisms of toxicity. On day one an hour was dedicated to the safety profile of Zydelig, adverse event management and the patient with questions and answers on these topics. In addition, there was 45 minutes given to three clinical cases in patients with CLL and FL, describing the adverse events and its management. On day two there was 35 minutes dedicated to the mechanism of action of Zydelig and its immune-mediated events.

Throughout the meeting, only 25 minutes were dedicated to the efficacy of Zydelig in the pivotal clinical trials. Indeed an hour was dedicated to the safety profile and safety management of Zydelig. The clinical cases presented provided a good balance between the efficacy and safety of Zydelig and how patients on Zydelig should be managed. Furthermore, on day two, the sessions on the mechanism of action provided the rationale for the efficacy as well as for the observed adverse effects with Zydelig.

On the topic of balance of the meeting, there were several instances where information on the mechanism of action and activity of competitors were discussed, as detailed below:

- the role of Bruton's tyrosine kinase (BTK) on the microenvironment and on the malignant B-cell as well as the implications of BTK inhibition
- the mechanism of action of the three targeted agents approved in CLL.

There was opportunity for exchange of information, the audience was invited to contribute to the session and to challenge or affirm the presented information. At the end of each data presentation there was time allocated for discussion, as follows:

- Zydelig safety profile: 25 minutes
- Adverse event management and the patient: 25 minutes
- Discussion: 10 minutes
- Masterclass: Analysing and critically appraising medical statistics: 1 hour
- Discussion: 15 minutes
- Zydelig mechanism of action: Immune-mediated activity and transformation: 20 minutes
- Discussion: 15 minutes
- Crosstalk: Genomic landscape of high-risk CLL and prevention of transformation
- Genomic architecture and clonal evolution in CLL: 25 minutes
- Prevention of Richter transformation: 25 minutes
- Joint discussion: 30 minutes
- Final questions and discussion: 10 minutes.

Overall, there were 90 minutes allocated to discussion between the attendees and the speakers to ensure the attendees were able to ask questions on any areas they did not fully understand. The feedback from participants did not indicate that any considered the meeting was inappropriate or not what they had expected, including the feedback provided by the new and existing UK Faculty members. Thus, Gilead did not consider that, in the context of a speaker training programme for Zydelig, the meeting was anything other than appropriate and the content was balanced and non-promotional. The company denied a breach of Clauses 7.2 or 12.1.

Gilead noted the complainant's comment that Zydelig was shown in a positive light, with doubt cast upon data perceived as negative for the medicine, and that competitors were disparaged and his/her reference to a statistics lecture. In response, Gilead stated that in line with the objective of the meeting identified above, the statistics lecture presented by an expert statistician was designed to provide the participants with the knowledge necessary to fully understand the statistics of medical studies, in particular as they related to key studies in this therapeutic area so that they could present clinical data accurately when engaged by Gilead to do so.

The presentation contained many case examples related to the topics discussed including those related to Zydelig and its competitors in the trials. These examples were provided as real-life case studies to statistical principles being discussed by the presenter. Multiplicity considerations were discussed with the goal of understanding the meanings of statistical significance, nominal significance and clinical meaningfulness. The statistical robustness of a competitor study or the fact that it achieved its primary endpoint was never questioned. With regard to the secondary endpoints, it was clarified by the presenter (as shown on the slides) that the improvement in overall survival was nominally significant and considered clinically meaningful by the authors. This information was accurate, balanced, was fair, and could be substantiated. Gilead disagreed with the complainant and thus did not consider that the lecture was promotional or that it disparaged other medicines. Gilead thus denied breaches of Clauses 7.2, 7.3, 7.4, 8.1, 12.1.

With regard to the complainant's criticism of the co-chair, Gilead explained that in addition to keeping the meeting running on time, the co-chair invited attendees to participate in the training and this could be welcomed especially when there were silences or natural pauses.

In relation to the complainant's allegation about the co-chair's remark about one competitor, Gilead stated that it was difficult to respond specifically as the company had no recollection of him/her making any statement about the competitor at the meeting and this was not included in the report of the meeting. In any event the co-chair did not intend to disparage other medicines and in relation to the statement on a second competitor, this was a statement of fact, the reference for which was provided.

The internal report of the meeting confirmed that the comment on the incidence of infections with a competitor was made in the context of an unsolicited question from one of the attendees about the use of Zydelig or the competitor in patients with liver disease or smoking-related lung disease. The pertinence of this question was founded on the risk of transaminitis and pneumonitis seen with Zydelig. One of the speakers responded and clarified that it was currently not clear whether smoking-related lung problems increased the risk of pneumonitis in patients receiving Zydelig, so in these patients any of the small-molecule therapies could be considered. The co-chair alluded to the topic of infections due to the risk of community-acquired pneumonia in patients with smoking habits, which could be aggravated by the increased risk of infections (including pulmonary) observed with Zydelig. To be fair and balanced, the co-chair mentioned that infections, including pneumonia, had also been observed with a competitor. In fact, infections with the competitor were mentioned in its summary of product characteristics (SPC) as a very common adverse drug reaction (≥ 1/10) and referred to in the section 'Special warnings and precautions for use'. Pneumonia, upper respiratory tract infection and sinusitis in particular were each mentioned as very common (≥ 1/10) drug reactions with the medicine. As could be attested by the SPC provided, this comment was accurate, balanced, fair, and could be substantiated.

Again, the co-chair did not intend to disparage other medicines, nor did he/she do so. The discussion was in response to a question, was balanced and reflected the most recent evidence available. Gilead denied breaches of Clauses 7.2, 7.3, 7.4, 8.1 and 12.1.

Gilead noted the complainant's comment that the co-chair asked questions that would result in the positive discussion of Zydelig, including discussions of off-label data, and appeared to deliberately support and build a favourable image of Zydelig.

Gilead considered that the discussions on the RIALTO study were in the context of an unsolicited question raised by one of the attendees on the availability of data about the maintenance of off-treatment response in patients who stopped Zydelig due to adverse events. An anecdotal clinical case

had been presented before this discussion. As there was no on-label information that could be shared about this topic, the co-chair invited one of the speakers to comment on one of his/her studies where a similar situation occurred: patients were treated with Zydelig for a median of 2.5 months and stopped treatment due to a safety signal. Published data on this study demonstrated that the patients treated with Zydelig for a median of 2.5 months had not progressed quickly, as seen in the progression free survival K-M curves (Pettitt, *et al* 2017). Gilead noted that the treatment in this study was stopped in the context of a safety signal observed in the previously mentioned three clinical trials sponsored by Gilead in 2016. Indeed, the treatment in the RIALTO study was not stopped due to data emerging from that particular trial, as could be implied from the complaint. The intent was solely to respond to an unsolicited question and to clarify the outcomes after stopping Zydelig treatment in this study and not to induce the prescription of Zydelig as per the inclusion criteria of RIALTO.

As per the meeting report, Gilead's answers in response to individual enquiries from members of the audience, were accurate, not misleading and it was clearly mentioned it was off-label and the response was restricted to that necessary to answer the question and ensure the attendee had a clear understanding of the relevant data for Zydelig. Understanding and recognising off-label data was important so that those engaged to speak on Gilead's behalf could do so compliantly in line with the instructions it gave on handling off-label questions.

Gilead stated that it provided clear guidance to those it engaged to speak about its products and in particular provided guidance on how to handle off-label questions that came for the audience. This guidance was presented to attendees on day one.

Gilead denied breaches of Clauses 3.2, 7.2, 7.3, 7.4, 9.1 and 12.1.

In response to the complainant's allegation that Zydelig was positioned as preventative treatment for Richter's transformation (RT) in CLL, Gilead explained that on day two a presentation 'Prevention of Richter transformation' from a globally respected expert haematologist informed participants about the unmet clinical need in CLL patients who progressed with Richter's transformation, an aggressive lymphoma transformation of CLL which occurred in approximately 3-10% of relapsed/refractory CLL patients. These patients had very limited treatment options with survival lasting only for a few months after conventional treatment.

Details of the presentation were provided.

The session trained participants to respond appropriately if asked about this topic when delivering Zydelig presentations. This was a topic of importance in the community (Khan *et al* 2018) and questions on it could be anticipated when members of the faculty presented in their subsequent speaker engagements.

As with all difficult to treat conditions, exploration of different strategies was rightly required in clinical trials. The speaker made it absolutely clear what the hypotheses were and what remained to be tested in prospective clinical trials. Gilead agreed with the complainant that different rates of Richter transformation had been noted with different novel agents so far and that indirect comparisons were always confounded as trial populations were different.

The speaker emphasised at the start of his/her presentation that he/she considered the best way to prevent Richter transformation was to treat CLL effectively, which considered all available therapies including conventional chemotherapy and novel agents. In this session, Zydelig was discussed for the treatment of CLL patients with high-risk disease, which included patients at risk of progression to Richter's transformation. Currently there were no biomarkers that could predict which patients would progress to Richter's transformation and when. These patients were treated, as any other CLL patient, with the treatments that were currently available, including Zydelig. The treatment of patients with CLL with high-risk was within the indication of Zydelig in CLL patients. Zydelig was not discussed for the treatment of Richter's transformation. Gilead did not 'position' Zydelig as preventive treatment to Richter transformation or as treatment for this condition and this session was provided in order that participants could address anticipated reactive questions on this topic in an informed manner in line with the guidance given on handling questions relating to off-label data. Gilead noted the complainant's objection to the inclusion of off-label data, but stated that this was considered necessary to ensure a complete and balanced position was provided to the participants, especially in relation to matters of safety. Gilead denied breaches of Clauses 3.2, 7.2, 7.3, 7.4, 8.1, 9.1 and 12.1.

With regard to the complainant's allegation that the hypothesis that Zydelig was an immuno-oncology compound which suppressed the high-risk clones, was presented as fact with no supporting data, Gilead stated that it had no recollection or record of this being stated at the meeting. Gilead submitted that the reference to a table being shown was likely to be a reference to a slide shown by the expert haematologist and, in that regard, its response on that slide was as stated above. Gilead denied breaches of Clauses 3.2, 7.2, 7.3, 7.4, 9.1, 11.1 and 12.1.

With regard to the number of Italian attendees, Gilead explained that in line with Italian requirements, the arrangements for the meeting, including the agenda and details of the Italian health professionals attending, were submitted for review by the Italian Medicines Agency (AIFA) and approved before the meeting took place.

All attendees were chosen based on the selection criteria referred to above. Having applied these criteria, the Italian Faculty members (new and existing) were invited to register for the meeting and the number registering to attend from Italy was higher than from any other countries. All met the criteria, and all wanted to maintain up-to-date knowledge so that they could speak accurately when presenting to other health professionals. The Gilead Oncology Faculty was a pool of trained speakers

who might be engaged by any country in the region to present on the topics covered by the Faculty, not just in their country of practice.

Zydelig was launched in Italy a few months before the safety signal emerged in March 2016 and when the Italian clinicians had little experience in managing the adverse events with Zydelig. Since then, the Gilead Oncology Faculty had been an important platform to train speakers who had then educated Italian clinicians on the appropriate use of Zydelig. Gilead considered that this initiative had positively contributed to the appropriate management of Zydelig and ultimately to the safety of patients.

Accordingly, Gilead considered that the arrangements for this training meeting were appropriate, including the appropriateness of each of those attending, and specifically each of the Italian attendees. All participants invited met the strict criteria set. The company did not consider that it had breached any clause of the Code in relation to this aspect of the complaint and in particular considered that the requirements of Clauses 11.1 and 12.1 had been met.

In conclusion, Gilead considered that GSEL's arrangements for the meeting met all the requirements of the Code. The event was an appropriate training meeting held to ensure health professionals GSEL intended to engage to speak on its behalf had a full and detailed understanding of the data set so that when they presented at Gilead organized meetings they could present the data in a way that reflected the evidence for Zydelig in line with its marketing authorization. Attendees were selected on clear and appropriate criteria and were told about the nature and purpose for the meeting through the invitation process. The attendees were not paid to attend unless they were engaged to present at the meeting.

In the light of its detailed response on all issues raised by the complainant, GSEL considered that it had adopted high standards in its arrangements for the meeting and did not accept that the arrangements were such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry. The company thus denied breaches of Clauses 2 and 9.1.

**FURTHER INFORMATION FROM GILEAD**

Gilead submitted that two UK delegates were invited to the meeting and each was invited directly by email. One of the delegates was nominated to be invited as a new faculty member by the UK head office based on certain criteria in particular that the UK team planned to engage him/her in Gilead sponsored meetings in 2018. The other UK delegate was an existing faculty member and so invited to update the training he/she first received in 2017. The UK team nominated him/her to attend based on a continued intention to engage him/her to speak on Gilead's behalf.

GSEL provided written and verbal guidance for staff throughout the preparations for the meeting. Information to the countries on the meeting was provided in the form of emails to the EMEA region and country specific e-mails, including guidance on speaker selection and invitation and monthly update calls organised by GSEL with the countries to provide updates, guidance, and request feedback from the countries (the Oncology Network Meetings). At the meetings the guidance in relation to the nomination and invitation process was given verbally.

- Reminder that the Gilead Oncology Faculty was the oncology speakers' programme and that the meeting was an opportunity to train new Faculty members or retrain existing members. Request for teams to nominate new Faculty members, who should attend on both days of the meeting. The country teams should contact the new Faculty members to explain the programme and assess their interest and availability for subsequent speaker engagements, and the agency would follow up with the clinicians with a formal invitation. Request for the team to identify existing Faculty members who they would like to invite to attend Day 2 only for update training. An option was given for the teams to either contact the existing members first followed by a written invitation by the agency, or the agency would contact the Faculty directly once nomination was received from the country team.

- Any nomination of new Faculty members should be local health professionals that the team already recognised as speakers and that they intended to engage in local/regional and the selection criteria (identified above) were set out.

Gilead provided copies of the UK attendees' agreements and gave details of when each had been engaged to speak on behalf of the company.

Gilead considered that the meeting was a non-promotional training meeting, but the presentations that trained faculty members subsequently gave could be promotional or non-promotional, depending on the content and context.

The statistician who also presented at the meeting and had not otherwise been engaged to speak in the last 12 months.

The Gilead UK Oncology team organised two types of meetings for health professionals – (i) regional meetings for which Gilead engaged as speakers faculty members who were leading experts; and (ii) localised meetings for which Gilead typically engaged newer faculty members. Shortly after the meeting was held, Gilead changed its priorities and organisation resulting in the field team in the region where two delegates were based being reduced to one medical scientist. Local meetings were consequently no longer being organized and the focus had been on regional meetings only. These changes were not foreseen when the meeting in question was held.

Gilead submitted that the faculty members who had not been engaged to speak did not still have access to the portal. In fact, no members of the faculty currently had access to the portal; Gilead was providing the necessary documents from the portal

to speakers as and when they were engaged to present on behalf of the company.

Gilead stated that the attendees were trained during the meeting on GSEL's requirements in relation to sharing any off-label data, and how to appropriately handle any unsolicited questions on off-label data that might arise when they were engaged to speak.

Guidance on handling unsolicited off-label questions from the audience in Gilead sponsored events was presented by Gilead on day one of the meeting under the topic 'Speaker engagements'. The presentation specifically mentioned that responses to unsolicited off-label questions needed to be objective, balanced, scientifically rigorous, and within the scope of the question. Once a concise answer limited to the scope of the question was provided, the speaker should immediately return to the approved presentation.

The speakers were also reminded that if they were informed of any off-label use of Gilead products, they were required to report that safety information to Gilead within 24 hours of becoming aware of the event.

**PANEL RULING**

The Panel noted that the meeting in question took place in Germany and was organised by the UK based affiliate, Gilead Sciences Europe. The Panel noted that the meeting had to comply, *inter alia*, with the UK Code. The Panel noted that the UK company, Gilead Sciences Limited, was responsible for the acts and omissions of its UK based European affiliate that came within the scope of the Code. The Panel noted that Gilead Sciences Europe had responded to the complaint.

The Panel noted Gilead's explanation that the Gilead Oncology Faculty was a register of trained speakers. The Panel noted the title of the meeting, Gilead Oncology Faculty meeting, and queried whether it fairly reflected the stated purpose of the meeting. In the Panel's view such faculties were often used to describe company convened meetings of key opinion leaders and such like. The impression given by the title of the meeting was important.

The Panel noted Gilead's submission that the meeting in question was an appropriate training meeting to ensure that health professionals whom the company intended to engage to speak on its behalf had a detailed understanding of the clinical dataset. The Panel considered that training speakers was an important and legitimate activity; the overall arrangements and content had to comply with the Code. When determining whether the content was appropriate the Panel considered that the overall arrangements, the therapy area and the professional status of the delegates were relevant. In the Panel's view it should be made clear to delegates at the outset and prior to their attendance that the meeting in question was a speaker training event and that they would be engaged as speakers thereafter. The Panel noted that speaker contracts were covered by Clause 23 which applied to contracts with consultants. The Panel considered that in principle it was good practice when training speakers to fulfil future speaker engagements to ensure that a written agreement covered the training activity to ensure that the arrangements including the nature of the meeting, the context in which data was presented and the parties' responsibilities and relationship were clear. Such written agreements were particularly important if the material disseminated referred to off-licence data so that the context of such references was clear. The Panel noted that there was a difference between interacting with a health professional as a prescriber and interacting with a health professional as a consultant. The Panel noted that if a company was interacting with a health professional in his/her capacity other than as a prescriber, such as training a health professional to speak on behalf of a company, such interaction might be considered non-promotional. In such circumstances, and where directly relevant, the provision of relevant unlicensed data to the health professional as part of such interaction might not be contrary to the provisions of Clause 3 which prohibited the promotion of unlicensed data or data that was inconsistent with the terms of a product's marketing authorization. The provision of such data to individuals who were training to be speakers should comply with the Code.

In relation to the meeting in question the Panel noted that no monies were paid to delegates who were not also presenting at that meeting. The Panel noted that the contract for UK delegates was headed 'Support for individual attendance at an event' and covered the quantification and disclosure of financial support to attend the meeting and its subsequent publication as a transfer of value. The contract did not refer directly or indirectly to a training event and appeared, in the Panel's view, akin to a contract for sponsorship to attend a clinical meeting as a delegate. The Panel noted its comments above about the impression given by the title of the meeting.

The Panel noted that attendees comprised health professionals who were existing members of the Faculty and who, unless presenting at the meeting in question, were invited for the second day, and new members who were invited to attend both days. The first day of the meeting was also open on an optional basis to existing members of the Faculty. The Panel did not have copies of the training materials on presentation skills.

The Panel queried whether the purpose of the meeting was sufficiently clear at the outset to all who were invited to attend, particularly as new faculty members. The Panel noted the invitation emails to the two UK participants dated 3 January (a returning faculty member) and 6 February 2018 (a new faculty member). The subject heading read 'Register for the meeting: Gilead Oncology Faculty Meeting, Frankfurt, 19-20 March 2018' and the first line of the email thanked the recipient for their interest in participating in the Gilead Oncology Faculty meeting (6 February) and their ongoing participation (3 January). The meeting was described as an interactive meeting which would 'provide training on idelalisib treatment and patient management, analysing medical statistics and practical presentation skills.' The opportunity for discussion with international

experts was referred to. The two day agenda was summarised in the body of the email; each day's summarised agenda referred to presentation skills training at the very end of a detailed list of clinical and statistical presentations. In the Panel's view the emails were not sufficiently clear that the primary purpose of the meeting in question was to train recipients of the emails as speakers and that the clinical data was presented for that purpose, rather they gave the impression that it was an invitation to attend a meeting about oncology therapy and idelalisib, part of which would include presentation skills training. In the Panel's experience it was not necessarily unusual for a clinical programme to include soft skills training such as presentation skills. The detailed agenda was attached to the email; day 1 had a 1.5 hour session on presentation preparation and a 10 minute session on speaker engagements; day 2 included 2 hours of presentation delivery/chairing skills. Whilst some details about the presentation skills sessions were given in the detailed agenda, the agenda still appeared primarily to describe a clinical meeting and did not negate the otherwise misleading impression about the primary purpose of the meeting given by the invitation emails. The reference to the faculty programme in the invitation and agenda implied that there was an ongoing clinical programme.

The Panel noted Gilead's submission about the selection criteria. The Panel did not know when the UK delegates had first been contacted to attend the meeting but noted that the email dated 26 July 2017 from the European company to local affiliates including the UK asked affiliates to nominate local health professionals. In the Panel's view that email implied that the primary purpose of the meeting in question was to enable delegates to acquire in-depth clinical knowledge, including about idelalisib. The list of 6 benefits of faculty membership, which one might reasonably assume that affiliates would highlight to potential invitees, included access to the faculty online portal which included a full idelalisib slide deck, case studies, the ability to create or download presentations, watch webcast presentations and symposia footage and the ability to submit questions. The final benefit referred to the opportunity to be invited to participate as a speaker at Gilead supported non-promotional events. In the Panel's view, the list of 6 benefits was inconsistent with Gilead's submission that the data at the meeting in question was presented in preparation for those invited to be engaged as speakers. The list of benefits made it clear that the portal material could be used for personal benefit unrelated to speaking at Gilead meetings. The email also referred to the opportunity to network and share clinical experience. The Panel acknowledged that the email dated 26 July did refer to training and speakers but considered that overall this was not given sufficient prominence; training was presented as just one of several benefits of the meeting. The Panel considered that it was supported in this view by the rationale for selection subsequently given by the UK affiliate in its email dated 1 December 2017 to the European company which nominated 12 new and 8 current members to attend the meeting in question and stated 'HCP with a special interest in FL/CLL who have engaged Gilead for educational support; HCP looking to extend their clinical knowledge and experience with targeted therapies'; suitability as a speaker and intention to engage them was not mentioned. The European company then asked the UK affiliate to approach the new members personally to explain the programme and what to expect and asked the UK affiliate to confirm that it planned to engage these new members as speakers in 2018. The UK company subsequently confirmed that 'the plan is to engage the HCP'. There was no evidence before the Panel that UK health professionals had been so informed. The Panel accepted that subsequent email correspondence from Gilead Sciences Europe to affiliates dated 29 November 2017 requesting case study nominations did refer to attendees as local speakers the affiliates were working with or were planning to work with.

The Panel noted the complainant's allegation that he/she had been invited to attend a non-promotional meeting and that before the meeting it was not made entirely clear that the premise of the meeting was to train speakers, and the content of the meeting was disguised promotion. The Panel considered that the primary purpose of the meeting should have been made abundantly clear at the outset when nominated individuals were contacted. Given the equivocal instructions to affiliates on this point as set out above in the email dated 26 July 2017, subsequent communications between the European affiliate and UK affiliate and its concerns about the invitation to UK delegates, the Panel did not understand how Gilead could be confident that all participants and, in particular, UK participants who had not previously attended a faculty meeting were clear from the outset that the meeting in question was a speaker training meeting. The Panel noted the complainant's comments on this point. The Panel considered, given its comments above, that on the balance of probabilities Gilead had not been unequivocally clear about the primary purpose of the meeting such that on arrival at the meeting an attendee who had not previously attended such meetings might consider that its stated true purpose, a training event, had, on the balance of probabilities, been disguised.

The Panel noted Gilead's submission that the purpose of the meeting and expectations of delegates after the meeting were clearly communicated at the start of the opening address and regularly during it but considered that this was too late, particularly for those who were new to the faculty and did not negate the failure to make the purpose clear to delegates prior to their arrival. The Panel considered that the failure to make the intended purpose of the meeting sufficiently clear at the outset meant that high standards had not been maintained. A breach of Clause 9.1 was ruled. The Panel noted its comments above about the impression given by the arrangements and considered that invitees would on the balance of probabilities consider that they were being invited to a promotional meeting and in this regard the Panel did not consider that the meeting was a disguised promotional activity and thus ruled no breach of Clause 12.1.

The Panel noted the complainant's allegation that the meeting was not balanced medical education and that subtle promotional techniques were used throughout the meeting. The complainant stated that examples were chosen of idelalisib in a positive light and competitors in a negative light and referred to the statistics presentation stating that examples were chosen to cast doubt on competitor data or data that could be perceived as negative for idelalisib, and that this was disparaging to one competitor in particular. The Panel noted that the statistics presentation entitled 'Analysing and critically appraising medical statistics' gave detailed explanations of statistical terms including several worked examples. A slide headed 'MURANO study ASH 2017' concluded that certain findings were exploratory only and could not be used as the basis for confirmatory claims. The Panel noted Gilead's submission that the statistical robustness of the study and that it achieved its primary endpoint were not put in question. The Panel noted the complainant bore the burden of proof and had not explained why the particular examples were disparaging. The Panel noted Gilead's submission that the presentation in question contained many examples including, *inter alia*, Zydelig and competitor trials. It was not always clear from the slides provided exactly what was discussed during the presentation of the slides in question. The Panel noted that the complainant bore the burden of proof. The Panel considered that the complainant had not provided sufficient detail to establish why the presentation in question was disparaging or an unbalanced comparison in this regard. No breach of Clauses 2, 7.2, 7.3 and 8.1 was ruled on this point.

The Panel noted that the complainant alleged that the co-chair was biased, examples referred to disparagement of competitor medicines. In relation to one particular competitor and infections, Gilead submitted that this was a statement of fact and referred to the infections listed as common in Section 4.8 of the relevant SPC. This listed four infections as very common, two as common and one as uncommon. The Panel noted that the summary Q&A for the meeting showed that in response to a question about the increased risk of transaminitis and pneumonitis in patients receiving idelalisib and management of certain patients a summarised answer read 'pulmonary infections have also been reported with other small molecule therapies, particularly [the competitor]'. The speaker was not identified in the summary but Gilead confirmed it was the co-chair who stated that infections including pneumonia had also been observed with the competitor. Gilead did not use the term 'particularly [the competitor]' in its response to this complaint. It was not clear precisely what had been said by the co-chair although it was clear that he/she had commented on the subject matter of the complaint. The Panel also noted Gilead's submission that the comments were made in response to an unsolicited question. Noting that the complainant bore the burden of proof, and Section 4.8 of the competitor SPC, the Panel considered that it had not been established that comments by the co-chair about the competitor were unbalanced. No breach of Clauses 7.2 and 7.3 was ruled on this point.

In relation to an allegation that the co-chair was biased as he/she questioned the validity of data on another competitor, the Panel noted Gilead's submission that it had no recollection of the co-chair making such a statement at the meeting and that this was reflected in the meeting summary. The Panel noted that the meeting summary did refer to discussion of the competitor data in response to questions, the identity of the speaker was not always clear but on the limited information before the Panel the responses in the meeting summary did not appear to question the validity of the competitor data as alleged. The complainant bore the burden of proof. The complainant had not identified the statements in question. The Panel considered that it had not been established that the validity of the data had been questioned as alleged. No breach of Clauses 7.2 and 7.4 was ruled.

The Panel noted the allegation that the Gilead co-chair deliberately asked questions of speakers so that positive idelalisib data would be discussed, including off-label data, and referred to a question to a speaker about the RIALTO study. The Panel noted Gilead's submission that the co-chair raised a question of a speaker to respond to an unsolicited question about the maintenance of off-label treatment response in patients who stopped idelalisib due to adverse events as a similar situation had occurred in that speaker's study and in a relevant anecdotal clinical case that had been presented by a different speaker prior to the discussion in question. The RIALTO study was subsequently referred to by the speaker in his/her response. The Panel had no detail about the case study but queried whether the question was, therefore, wholly unsolicited given the prior discussion and whether the company's response could truly take the benefit of the exemption to the definition of promotion in Clause 1.2, as implied by Gilead. The Panel noted that, contrary to the complainant's comments about the cessation of the study, Gilead submitted that it was stopped in the context of a safety signal observed in 3 different trials sponsored by Gilead. The Panel noted that both parties agreed that off-licence data was discussed. The Panel considered that it was not necessarily unacceptable to train speakers to respond to questions about off-licence data; whether it was acceptable would depend on a number of factors. The Panel noted its comments above in this regard. The Panel considered that given the product and therapy area, CLL and FL, speakers might be asked questions about unlicensed data and it was not unreasonable to train them to address such questions so long as, overall, the activity otherwise complied with the Code. The Panel noted that the complainant bore the burden of proof. The Panel noted its concerns above but, on balance, considered that there was insufficient evidence before it to determine whether Gilead had breached the Code on this matter. No breach of Clause 3.2 was ruled.

The Panel noted the allegation that idelalisib was being positioned as a preventative treatment for Richter's transformation in CLL and that there was no data to support these claims. The Panel noted

idelalisib's licensed indication in combination with rituximab or ofatumumab for the treatment of certain adult patients with CLL. The Panel noted its general comments above about the provision of data about the unlicensed use of a product as part of a formal speaker training event.

The Panel noted Gilead's submission that a presentation entitled 'Prevention of Richter's transformation' was provided to train participants on the clinical unmet need in patients with CLL who progress with Richter's transformation. Gilead also stated that the session was delivered to train participants to respond appropriately if asked about this topic when delivering presentations on idelalisib. The Panel considered that given the therapy area, in principle, it was not unreasonable, within the context of *bona fide* speaker training, to train participants to answer unsolicited questions about the off-licence use of a product. Context would be very important; it should be made clear that the provision of such data by a speaker during a promotional presentation should only be reactive and in response to an unsolicited question. That the speakers' response to an unsolicited question about the unlicensed use of a product should do no more that answer the question (and/or refer the question to medical information for a response) should be an integral part of any company's speakers' training presentation.

The Panel noted that the presentation in question 'Prevention of Richter's transformation' was delivered on the afternoon of the final day. The presentation described Richter's transformation and innovative trial designs to avoid clonal evolution in high risk CLL patients. Slides gave a clinical trial data overview and the incidence of Richter's transformation in certain patients treated with a competitor (six studies: 3-16%) and then idelalisib (nine studies: 2 - 2.4%). The Panel noted the summary slide described Richter's transformation as an unmet clinical need in CLL patients, referred to clonal evolution and stated that an understanding of the mutational landscape and pathways driving Richter's transformation may help define strategies to prevent transformation. The slide immediately preceding that summary was headed 'Idelalisib may prevent clonal evolution of high-risk CLL clones potentially resulting in the low rate of Richter transformation' which, in the Panel's view, implied that idelalisib might satisfy the unmet clinical need in Richter transformation referred to on the summary slide. The Panel noted the complainant's comment that the speaker said a number of times that any observed differences should be taken with a pinch of salt due to differences between the studies and a number of other factors. The Panel noted Gilead's submission about caveats made by the speaker during the presentation in relation to comparison of such data. The Panel noted that such caveats did not appear on the slides in question and considered that if such caveats were necessary for Code compliance the slides should be capable of standing alone in that regard. The Panel noted Gilead's submission that indirect comparisons with different novel agents were always confounded as the trial populations were different. The Panel had no way of knowing precisely what was said by the speaker. The summary of Q&A provided helpful guidance; a speaker, having noted the relatively low rates of RT with idelalisib, favourably compared idelalisib with its competitors and speculated on the effect that different modes of action might have. The presenter stated 'I consider the data highlighting differences in RT rates between different targeted therapies potentially practice changing in terms of how I use idelalisib in **CLL'** (emphasis added). The Panel noted that whilst both parties agreed that the speaker had outlined caveats in relation to indirect comparisons, this was not reflected in the summary Q&A. The Panel considered that other presentations were relevant to idelalisib and Richter's transformation. The presentation that immediately preceded that on Richter's Transformation, 'Genomic architecture and clonal evolution in **CLL**', included a section entitled 'Clonal Evolution in Richter's transformation'. A preceding presentation 'Idelalisib mechanism of action:Immune mediated-activity and transformation' detailed the product's mechanism of action and, in the Panel's view, highlighted features relevant to prevention of RT and idelalisib. The Panel considered that the overall narrative of the presentations was such that they highlighted features of idelalisib including its unique mechanism of action in relation to the prevention of RT which was described in the final presentation as an unmet clinical need. The Panel considered that the totality of the presentations, together with the description of such comparative data as 'potentially practice changing' by a globally respected expert was such that, on balance, the company advocated the use of idelalisib for prevention of Richter's Transformation. In the Panel's view, relevant caveats should have been an integral and prominent part of each slide in question and such caveats should be accurately reflected in the speaker's comments. In this regard, the Panel was concerned that the presentation had been available to download from the Faculty portal. The Panel considered that the presentations and comments by the speaker went beyond training a speaker to respond to an unsolicited question about a product and RT. In this regard, the Panel noted that a UK existing Faculty member had subsequently delivered promotional presentations which positively referred to idelalisib's mechanism of action in the context of the prevention of Richter's transformation. In the Panel's view, Zydelig was positioned as a preventative treatment for Richter's Transformation as alleged. A breach of Clauses 3.2 and 7.2 was ruled.

In relation to the complainant's allegation about an imbalance of delegates from Italy, the Panel noted Gilead's explanation, including that the product was launched in Italy a few months before the safety signal emerged in March 2016 and Italian clinicians had little experience in managing adverse events at that time. The Panel did not consider that the proportion of Italian participants alone rendered the meeting inappropriate as a training event. No breach of Clause 9.1 was ruled on this narrow point.

In relation to the allegation that Gilead accepted and verbalised the hypotheses about idelalisib being an 'immuno-oncology compound which supresses the high risk clones' without data to support such claims,

the Panel noted Gilead's submission that it had no recollection or record of this being verbalised at the meeting. The Panel noted that the comment, or one closely similar, did not appear in the summary of Q&A. The Panel therefore considered that the complainant, who bore the burden of proof, had not established that the statement had been made and, on this basis, ruled no breach of Clause 7.4 of the Code.

**Complaint received** **19 April 2018**

**Case completed** **3 June 2019**

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# ANONYMOUS CONTACTABLE v NOVARTIS

## Failure to publish joint working executive summary

**An anonymous, contactable complainant considered that a cancer data project, operating in a named Scottish region, appeared to be a joint working project although it had not been declared as such by the four companies involved including Novartis. The complainant stated that the ABPI had, *inter alia*, published news of the collaboration. The complainant had not seen relevant details published on Novartis' website, noting that an executive summary should be published before such projects start. If such details were on the website they were not visible and hence transparent – the project was not listed alongside Novartis' other joint working projects.**

**The complainant acknowledged that it might be a very positive joint working project but queried whether, as long as their project was endorsed by the ABPI, member companies did not have to comply with the Code. The complainant queried whether the ABPI was leading companies to flagrantly bypass the Code.**

**The detailed response from Novartis is given below.**

**The Panel noted that joint working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experience and/or resources for the joint development and implementation of patient centred projects and shared a commitment to successful delivery. The relevant supplementary information to the Code described the features of joint working including that it must be for the benefit of patients, but it was expected that the arrangements would also benefit the NHS and the pharmaceutical company or companies involved. The Code required a formal written agreement to be in place and an executive summary of the joint working agreement to be made publicly available before arrangements were implemented.**

**The first issue that the Panel had to decide was whether the arrangements referred to by the complainant constituted joint working.**

**To determine whether an arrangement was joint working one had to consider whether the project was for the benefit of patients. The Panel noted the benefits for all stakeholders listed in the protocol and considered that these were primarily, although not exclusively, for the benefit of patients. In the Panel's view, that there were ancillary benefits to pharmaceutical companies did not preclude the overall arrangements being considered a joint working project even if such benefits primarily influenced a company's decision to participate.**

**The Panel noted that, according to Novartis, the NHS region had not wanted to contract directly with the pharmaceutical companies and thus the contract was made with the ABPI. The Panel noted the sensitivities. The ABPI and the companies had discussed the classification of the project. Ultimately, and irrespective of such discussions, companies had to take responsibility for the project classification under the Code. In the Panel's view, it was clear from an overall evaluation of the contract between the NHS region and the ABPI, and between the ABPI and each individual company, that the ABPI was contracting on behalf of the four companies and the use of a third party did not, in the Panel's view, mean that the companies could circumvent the requirements of the Code. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.**

**In relation to the project at issue, its protocol set out benefits for stakeholders. Benefits for patients were listed first and described as 'Improved patient concordance, adherence and benefit from therapy through additional support of data to ensure optimal use of their medicines'; and 'Better information as a basis for patient specific treatment decisions'. The first two of three benefits for the regional NHS board were relevant to patients and included an audit framework as a basis for improved quality of care for breast cancer patients across a Scottish region and 'Improved capture of patient outcomes'. The four benefits to ABPI/industry included 'Improved reputation by working jointly with NHS to benefit patients' and 'The optimal use of medicines in the appropriate patients which should mean better proactive treatment and management of patients'.**

**The Panel noted that the four companies had each paid £32,480.50 and that the ABPI SCG had paid £10,000 towards the project giving a total of £139,922. The NHS had contributed £118,309.50. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.**

**The Panel noted Novartis' submission that the project was a joint industry and NHS collaboration. Novartis had certified the protocol as joint working as it considered this was the closet fit to the nature of the project. The project included features of joint working, namely: industry and NHS resources had been pooled to implement a project for the benefit of patients; outcomes that would also benefit the NHS and the four companies involved; both the health board and the four companies had made significant financial contributions towards the project and defined project outcomes were to be measured and documented. However, not all of the benefits for stakeholders as set out in the protocol were for the benefit of patients. The Panel noted its comments above in this regard and considered that the benefits as listed in the protocol in relation to Phase 1 of the project could be predominantly characterized as for the benefit of patients. The Panel considered**

**that the arrangements at Phase 1 of the project in relation to the NHS region were a joint working project and thus an executive summary of the written agreement ought to have been published before the arrangements were implemented. The Panel ruled breaches of the Code including that high standards had not been maintained. In the Panel's view, the circumstances did not warrant a ruling of a breach of Clause 2 which was reserved to indicate particular disapproval of a company's activities and reserved for such use. No breach of Clause 2 was ruled.**

**The four pharmaceutical companies involved in the above project were each subject to a complaint. Novartis (Case AUTH/3043/6/18) and Roche (Case AUTH/3044/6/18) accepted the Panel's rulings of breaches of the Code. AstraZeneca (Case AUTH/3046/6/18) and Pfizer (Case AUTH/3045/6/18) appealed those rulings.**

**At the appeals of Case AUTH/3045/6/18 and Case AUTH/3046/6/18 on 17 January the Appeal Board noted that although the whole project (Phases 1-3) included features of joint working the protocol of agreement between the four companies and the NHS region was limited to completing Phase 1. The outcomes of Phase 1 were data centred rather than patient centred. The Appeal Board considered that the arrangements at Phase 1 of the project in relation to the NHS region were not a joint working project and thus no executive summary of the written agreement needed to have been published before the arrangements were implemented. The Appeal Board ruled no breaches of the Code.**

**After the consideration of the appeals by AstraZeneca and Pfizer the Appeal Board agreed that Novartis and Roche should be contacted and informed of the outcome. The PMCPA Constitution and Procedure did not cover this unusual situation where more than one company was involved in the same set of circumstances and the Appeal Board had taken a different view to the Panel. Novartis and Roche were each offered the opportunity to appeal out of time. The complainant was also informed. Roche declined the opportunity to appeal. Novartis accepted the option to appeal.**

**In addition to the submission from Novartis the Appeal Board noted relevant elements of its rulings in its consideration of the appeals from Pfizer (Case AUTH/3045/6/18) and AstraZeneca (Case AUTH/3046/6/18).**

**The Appeal Board considered that the documents could have been better worded to more accurately reflect the arrangements and this included the information issued by the ABPI.**

**The Appeal Board noted Novartis' submission that it had the necessary documents certified using the Novartis joint working Zinc job category as it was the closest fit to the collaborative and non-promotional nature of the project. Novartis did not consider that the project was a joint working project. Novartis considered that the arrangements relating to the project were in line with the requirements of Clause 21 of the Code.**

**The Appeal Board noted that the whole project included features of joint working, namely, the pooling of industry and NHS resources to implement a project with outcomes listed in the protocol for the benefit of patients and the benefit of the NHS and the four companies involved including Novartis; both the Scottish region health board and the four companies including Novartis had made a significant financial contribution towards the project; and defined project outcomes were to be measured and documented. However, the Appeal Board noted that the protocol of agreement was limited to completing Phase 1. The outcomes of Phase 1 were a data dictionary, a data quality report and example epidemiological, clinical pathway and outcomes reports that would be aggregated and anonymised and only available to the companies when they had been published by the NHS region. Although referred in the protocol, Phases 2 and 3 were not part of the current protocol of agreement and there was no agreement or obligation that the company would be involved in them.**

**The Appeal Board noted that Novartis in its appeal provided better and further particulars than had been provided to the Panel particularly with regards to the actual outcomes of Phase I. Pfizer (Case AUTH/3045/6/18) and AstraZeneca (Case AUTH/3046/6/18) also commented on the misleading nature of the ABPI press release at their appeals.**

**The Appeal Board noted that its role was solely to determine whether the activity at issue was joint working thereby triggering the requirement to publish an executive summary.**

**The Appeal Board noted that although the whole project (Phases 1-3) included features of joint working the protocol of agreement between the four companies and the NHS region was limited to completing Phase 1. The outcomes of Phase 1 were data centred rather than patient centred. The Appeal Board considered that the arrangements at Phase 1 of the project in relation to the NHS region were not a joint working project and thus no executive summary of the written agreement needed to have been published before the arrangements were implemented. The Appeal Board ruled no breaches of the Code . The appeal on both points was successful.**

An anonymous, contactable complainant considered that a cancer data project operating in a named Scottish region appeared to be a joint working project although it had not been declared as such by the four companies involved, including Novartis.

The complaint was taken up with all four companies including Novartis.

**COMPLAINT**

The complainant stated that in May 2018, the ABPI had, *inter alia*, published news of the project in question.

The complainant queried whether the project was a joint working project with the NHS. If that was the case, the complainant had not seen details published on Novartis' website, noting that an executive summary should be published before such projects started. If details were on the website they were not very visible and hence transparent – the project certainly was not listed alongside Novartis' other joint working projects.

The complainant noted that the ABPI news alert stated that funding of the project from the region was being matched and queried whether matched funding was one of the principles of joint working.

The complainant acknowledged that it sounded like good news and it might be a very positive joint working project but queried whether, as long as their project was endorsed by the ABPI, member companies did not have to comply with the Code. The complainant queried whether the ABPI was leading companies to flagrantly bypass the Code.

When writing to Novartis, the Authority asked it to consider the requirements of Clauses 2, 9.1 and 20.

**RESPONSE**

Novartis explained that the cancer data project was an ongoing collaboration between a named health board and ABPI that sought to drive adoption of real-world electronic health data relating to current care pathways and patient populations, and to better incorporate such data into health technology assessment (HTA) processes by developing a reproducible, data-driven regional cancer technology evaluation framework. The project aimed to drive improvement in health outcomes, to introduce new models of technology with evidence development and commercial value reimbursement models, and to support the improved use and optimization of medicines. Ultimately, the expectation was that these data-driven improvements would benefit patients in the future by leading to improved patient concordance, adherence and benefit from their therapies, and via the generation of better information as a basis for patient-specific treatment decisions. The project focus was on the breast cancer patient pathway, and the adoption of this pooled real-world data would drive a clearer understanding of the best treatment pathways in breast cancer.

The project started on 20 April 2018 and would last for 18 months. A copy of the project protocol which described the project in detail and set out the benefits of the participating parties was provided.

The project deliverables were:

- To develop a clear understanding of what data existed, and the quality of the data across primary and secondary care within the NHS region, and determine whether these data could be linked to create a data framework;
- To develop a breast cancer data framework;
- To produce publicly available end of milestone reports. The report generated at the end of milestone 3 of the project would seek to demonstrate the robustness of the breast cancer data framework;
- The development of a process within the NHS region for the pharmaceutical industry to engage with and access reports using the new breast cancer data framework; and
- To consider next steps at the conclusion of the project and to consider whether a second project could be explored which would expand the scope of the project regionally and from primary and secondary care to other data sets that looked at societal benefits.

A clinician from the NHS region in question initially contacted the ABPI about the project through Novartis in August 2016. The project was a collaboration between the ABPI and a named health board and was funded by four members of the ABPI Scotland Collaborations Group (SCG), namely Pfizer, AstraZeneca, Roche and Novartis in the sum of £32,480.50 per member, and by the ABPI in the sum of £10,000 (equating to a total industry contribution of £139,922). The total contribution from the NHS towards the project was £118,309.50. A copy of the signed Contribution Agreement and Trade Mark Licence dated 13 March 2018, which set out the contractual terms relating to this project, was provided.

Novartis explained that in return for their funding of the project, an ABPI SCG representative and representatives from the four companies were entitled to attend project steering group meetings in order to monitor implementation of the project and to report back on project progress to the wider ABPI SCG. Additionally, the ABPI SCG could input into the project by advising the NHS region on external communications elements in relation to the project. Further, on completion of the project, the four group members would also be able to pilot the new process of accessing the NHS regional real-world data (an outcome of the project) by asking the data framework questions set out in the project protocol provided. The four group members might use the authors of those questions to support future health technology appraisal (HTA) submissions.

For the avoidance of doubt, the project used existing data within the NHS specific region. The ABPI SCG and the four group members would only see anonymised (ie non-identifiable) and aggregated data.

**Classification of the Project**

Novartis submitted that the project was a joint industry and NHS collaboration which included some features of joint working, namely:

- The pooling of industry and NHS resources to implement a project for the benefit of patients;
- Outcomes would also benefit the NHS and the ABPI (and the four group members);
- Both the named health board and the ABPI made a significant financial contribution towards the project; and
- Defined project outcomes were to be measured and documented.

However, the project benefits were not explicitly focused on patients, but rather on helping the NHS to use Electronic Health Care Record Data whilst also helping the pharmaceutical industry to explore the potential for a Breast Cancer Data Framework to help HTA research. This took the project outside the scope of joint working arrangements covered by Clause 20. There were several other reasons why this project was not classified as joint working by the ABPI SCG.

Firstly, at the project concept phase, certain stakeholders within the NHS region stated that they would only collaborate and contract with ABPI Scotland in relation to the project; they did not want to contract directly with the four industry members of the ABPI SCG. The proposal went to the ABPI for comment and it was recommended that the project should be overseen by the ABPI SCG. It was decided at an ABPI SCG meeting that the ABPI (which would also make a financial contribution towards the collaboration) would enter into the relevant agreement on behalf of the ABPI SCG.

The four group members saw the benefits in the increased adoption of real-world electronic health data and wanted to contribute financially to the ABPI towards its participation in the project. The ABPI supported this approach. It was hoped that participation in the project would raise the profile and credibility of the industry with healthcare organisations and the Scottish Government and would create future opportunities for collaborative working.

Whilst joint working under Clause 20 might have been a logical fit for this activity, the ABPI advised the four group members that – as an organisation – it could not enter into joint working agreements. The ABPI was satisfied that this was collaborative working between ABPI SCG and its external partners and it drafted a contract for consideration by the four group members.

An agreement drafted by the ABPI reflected the collaborative nature of the project and outlined the benefits received by the ABPI SCG and the four group members in return for their funding. The agreement was signed on behalf of the ABPI.

Before signing, each of the four group member companies sent a confirmation statement to the ABPI in which it confirmed that it was happy for the ABPI to contract on behalf of the ABPI SCG, namely by confirming:

> 'For and on behalf of [company name], I hereby authorise ABPI to enter into this contract on behalf of the ABPI Scotland Collaborations Group, and to pay for the contract using the Group's collected funds.'

The Novartis confirmation was provided.

**Classification of activity under the Code**

In Novartis' view, the project was not a medical and educational goods and services arrangement falling within the scope of Clause 19 because of the collaborative nature of the project and because the ABPI SCG and the four group members would get certain benefits in return for their funding (as outlined above).

Novartis considered that (for the reasons given above) the project could not be classified as joint working under Clause 20. However, Novartis noted that Clause 21 gave direction on how to manage 'other funding by the company not otherwise covered by the Code'. In line with the requirements of Clause 21, a letter of agreement dated 21 November 2017 had been signed by Novartis and the ABPI (copy provided). This letter of agreement also set out other terms relating to the provision of funding to the ABPI by Novartis, including the basis upon which the ABPI had entered into the agreement with the NHS region. Agreements made it clear that Novartis (and the other three group members) might publicly disclose the funding which they contributed to the total value transferred by the ABPI to the NHS region under the arrangements. Novartis would publish the funding on its website imminently as part of its 2017 funding disclosure exercise.

**Internal approval steps**

The project was fully reviewed and approved internally by Novartis, including by medical, compliance and legal functions. The project protocol was certified in Zinc (copy approved). Novartis did not have a Zinc job category to cover collaborative projects entered into by the ABPI (towards which it provided funding). It was therefore decided that a 'joint working' Zinc job category should be used for internal approval purposes as this was the closest 'fit' to the collaborative and non-promotional nature of the project. However, it was clearly stated in the job summary within Zinc that this project was an ABPI Collaboration Agreement and not joint working. The job summary was provided. An executive summary was not published on the Novartis website as this was an ABPI-contracted project that had not been classified externally as joint working.

**Novartis' response to the complaint**

Novartis submitted that whilst including some features of joint working, the project was not structured as joint working, but as a collaboration arrangement under the guidance of the ABPI.

Novartis noted that Clause 21 gave direction on how to manage other funding by the company not otherwise covered by the Code. For the reasons described above, it was purposefully not set up as a joint working arrangement, including because the agreement that was put in place to govern the arrangements was entered into by the ABPI (and not the four individual pharmaceutical companies involved in funding the project) and the ABPI could not itself enter into joint working arrangements. There was no executive summary published because the arrangements were not structured as joint working, and the ABPI (rather than the four group members) was the contracting party to the agreement. Therefore, the provisions of Clause 20 relating to the publication of executive summaries did not apply to the four group members.

The project was fully reviewed and approved internally within Novartis and the necessary documents certified using the Novartis joint working Zinc job category as it was the closest fit to the collaborative and non-promotional nature of the project. Novartis considered that the arrangements relating to the project, including the entering into the Contribution Agreement and Trade Mark Licence by the ABPI on behalf of the ABPI SCG, were appropriate. In line with the requirements of Clause 21, Novartis would publish details of the funding it provided towards the project on its website imminently as part of its 2017 funding disclosure exercise.

Novartis denied a breach of Clause 20.

Novartis' involvement in the project (as a group member of the ABPI SCG) was reviewed and approved internally in accordance with the Code and relevant standard operating procedures (SOPs). Novartis considered that the project was a strong example of non-promotional collaborative working between the pharmaceutical industry and the NHS and that the highest standards were maintained throughout the design, approval and delivery of this innovative oncology-focused project. The ABPI and all four group members of the ABPI SCG agreed on the appropriateness of the classification of the project as a collaboration arrangement which would be entered into by the ABPI on behalf of the ABPI SCG.

Novartis denied a breach of Clause 9.1.

The project had the clear aims of driving improvements in health outcomes, introducing new models of technology with evidence development and commercial value reimbursement models, and supporting the optimisation of treatment options. The data-driven improvements which were the focus of this innovative project had the potential in the future to benefit patients by leading to improved patient concordance, adherence and benefit from their therapies, and by the generation of better information as a basis for patient-specific treatment decisions.

Novartis considered that its management of this project complied with Clause 21. The arrangement was put in place to provide funding for the health board to create the data framework and a model in which both industry and the NHS could use that data. The arrangements were managed via a collaboration coordinated by the ABPI and a contract was put in place with the ABPI. No other clause explicitly defined this type of collaboration.

With this in mind, Novartis considered that rather than bringing the industry into disrepute, the project was an example of collaborative working between the pharmaceutical industry and the NHS with the aim of enabling the NHS to use data more effectively and allowing industry to use the data to bring innovations to the market. Therefore, it served to improve industry reputation rather than to damage it. The generation and use of real-world data would be of significant and of increasing importance both in oncology and more broadly as the healthcare system looked to make more targeted patient-specific treatment decisions in the future, which in turn would drive improved patient outcomes. To this end, Novartis had received positive feedback on the nature of the project from multiple external stakeholders.

Novartis recognized that Clause 2 was a sign of particular censure, and as such was reserved for such circumstances. Novartis denied a breach of Clause 2.

**Conclusion and summary of Novartis' position**

Novartis denied any breach of Clauses 20, 9.1 or 2. Whilst the project included some features of joint working, it was structured as a collaboration arrangement between industry and the NHS. Whilst not expressly covered by the Code, Novartis treated this as a non-promotional collaboration, and it fully applied the principles of the Code in relation to this activity. In line with the requirements of Clause 21, Novartis would publish details of the funding it provided towards the project on its website imminently as part of its 2017 funding disclosure exercise. The agreement which governed the project arrangements was entered into by the ABPI. An executive summary was not published on the Novartis website as this was an ABPI-contracted project that had not been classified as joint working, and so the provisions of Clause 20 relating to the publication of executive summaries did not apply.

Novartis stated that as a result of this complaint, it would publish on its website executive summaries of all ABPI-led sub-group collaboration arrangements with which it engaged in the future. It would also investigate the addition of a new certification category of collaboration arrangements to its internal Zinc approval system.

**PANEL RULING**

The Panel noted that joint working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experience and/or resources for the joint development and implementation of patient centred projects and shared a commitment to successful delivery. This definition was reproduced in the supplementary information to Clause 20 Joint Working. The relevant supplementary information to Clause 20 then described the features of joint working including that it must be for the benefit of patients, but it is expected that the arrangements will also benefit the NHS and the pharmaceutical company or companies involved. Clause 20 required a formal written agreement to be in place and an executive summary of the joint working agreement to be made publicly available before arrangements were implemented.

Thus, in the Panel's view, it was clear that joint working would produce benefits to the NHS and pharmaceutical companies in addition to outcomes for the benefit of patients. That a joint working

arrangement produced other benefits including in relation to a company's commercial interests would not necessarily preclude the overall arrangement being classified as a *bona fide* joint working project.

The complainant alleged that certain companies had failed to publish an executive summary of joint working arrangements. The first issue that the Panel had to decide was whether the arrangements constituted joint working.

The Panel noted that the complaint concerned four pharmaceutical companies including Novartis. All four companies were members of the ABPI Scotland Collaborations Group (SCG). The Panel noted that although the complaint concerned the same project the companies gave differing accounts about some aspects of the project including its internal classification. Not all companies had provided all relevant documentation.

The Panel noted that the project protocol was set out in a document titled Data Intelligence for the Value Appraisal of Personalised Healthcare Technologies for Cancer within the [named] cancer Network, Version 9, Date of Preparation June 2017, which was appended to the agreement between the ABPI and the Scottish health board dated 13 March 2018. The version certified by Novartis was Version 10 and bore a Date of Preparation of August 2017. The background section of the project protocol explained that the parties had identified a need to provide a robust and prospectively designed technology adoption and evaluation framework to exploit rich routinely collected datasets for value assessment and evidence development in real world settings. The protocol explained that such data was needed by NHS decision makers and, *inter alia*, local service managers. It was noted that existing patient access schemes were inefficient and such data would also make possible more preferable population level schemes. It was also noted that there was potential for such data to be exploited by others including academic communities which relied on routine capture of electronic health data. The protocol explained that there was an urgent need to understand the detail of what was currently possible and what further developments needed to be undertaken. There were three geographical phases to the overall project: Phase 1 in relation to breast cancer patients and the NHS region; Phase 2 in relation to four health boards comprising the named cancer network; and Phase 3 was national in scope and broader than breast cancer and would be in collaboration with another organisation.

The project work plan including costings set out in the protocol was in relation to Phase 1 of the project only and had 3 milestones. Breast cancer data had been identified for Phase 1 of the project and hence the proposed collaboration with the NHS region health board which had a pre-existing data set. In the Panel's view the complaint was about this regional Phase 1 collaboration rather than subsequent phases of the project which were referred to but not detailed in the protocol. The funding provided was in relation to Phase 1 of the project.

In relation to the project at issue, the protocol set out benefits for stakeholders. Benefits for patients were listed first and described as 'Improved patient concordance, adherence and benefit from therapy through additional support of data to ensure optimal use of their medicines'; and 'Better information as a basis for patient specific treatment decisions'. The first two of three benefits for the NHS named health board were relevant to patients and included an audit framework as a basis for improved quality of care for regional breast cancer patients and 'Improved capture of patient outcomes'. The four benefits to ABPI/industry were listed as 'Improved reputation by working jointly with NHS to benefit patients', 'Improved professional and transparent relationship and trust between ABPI, Industry and NHS Health Boards', 'Access to anonymized aggregated data through public domain reporting to highlight the outcomes of the project to allow greater disease understanding' and 'The optimal use of medicines in the appropriate patients which should mean better proactive treatment and management of patients'.

Four sub-project work packages were listed and included direct-from-data clinical pathway modelling for outcomes estimation in support of, *inter alia*, cost-effectiveness modelling for Scottish Medicines Consortium Submissions and local business cases and expanding beyond NHS activity into social care. It appeared, although it was not entirely clear, that the sub work packages related to Phases (work packages) 2 and 3 rather than the phase in question.

In relation to Phase 1 of the project, the Panel noted the companies' and the NHS region's contributions as set out in the protocol. The Panel noted the companies' ongoing role on the steering committee. The Panel also noted Novartis' submission that the ABPI SCG could input into the project by advising the NHS region on external communications elements in relation to the project.

To determine whether an arrangement was joint working one had to consider whether the project was for the benefit of patients. The Panel noted the benefits for all stakeholders listed in the protocol and considered that these were primarily although not exclusively for the benefit of patients. In the Panel's view, that there were ancillary benefits to pharmaceutical companies did not preclude the overall arrangements being considered a joint working project even if such benefits primarily influenced a company's decision to participate.

The Panel noted that, according to Novartis, the NHS region had not wanted to contract directly with the pharmaceutical companies and thus the contract was made with the ABPI. The Panel noted the sensitivities. The Panel noted that there had been discussion between the ABPI and the companies about the classification of the project. Ultimately and irrespective of such discussions companies had to take responsibility for the project classification under the Code. In the Panel's view, it was clear from an overall evaluation of the contract between the NHS region and the ABPI, and between the ABPI and each individual company, that the ABPI was contracting

on behalf of the four companies and the use of a third party did not, in the Panel's view, mean that the companies could circumvent the requirements of the Code. The agreement between the ABPI and the NHS region dated 13 March stated at the section headed Compliance in relation to declaration of the companies' involvement in the project that ABPI SCG comprised four named companies including Novartis. The four companies were also listed alongside their financial contributions in an appendix to that agreement. The project protocol appended to the agreement did not name the companies, although the certified version did.

The Panel noted that the four companies had each paid £32,480.50 and that the ABPI SCG had paid £10,000 towards the project giving a total of £139,922. The NHS had contributed £118,309.50. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.

The Panel noted Novartis' submission that the project was a joint industry and NHS collaboration. Novartis had certified the protocol as joint working as it considered this to be the closet fit to the nature of the project. The project included features of joint working, namely: the pooling of industry and NHS resources to implement a project for the benefit of patients; outcomes that would also benefit the NHS and the four SCG group members; both the regional health board and the four SCG companies, including Novartis, had made a significant financial contribution towards the project and defined project outcomes were to be measured and documented. However, not all of the benefits for stakeholders as set out in the protocol were for the benefit of patients. The Panel noted its comments above in this regard and considered that the benefits as listed in the protocol in relation to Phase 1 of the project could be predominantly characterized as for the benefit of patients. The Panel considered that the arrangements at Phase 1 of the project in relation to the NHS region were a joint working project and thus an executive summary of the written agreement ought to have been published before the arrangements were implemented. The Panel ruled a breach of Clause 20 in this regard. High standards had not been maintained, a breach of Clause 9.1 was ruled. In the Panel's view, the circumstances did not warrant a ruling of a breach of Clause 2 which was reserved to indicate particular disapproval of a company's activities and reserved for such use. No breach of Clause 2 was ruled.

The four pharmaceutical companies involved in the above project were each subject to a complaint. Novartis (Case AUTH/3043/6/18) and Roche (Case AUTH/3044/6/18) accepted the Panel's rulings of breaches of Clauses 20 and 9.1. AstraZeneca (Case AUTH/3046/6/18) and Pfizer (Case AUTH/3045/6/18) appealed those rulings.

At the appeals of Case AUTH/3045/6/18 and Case AUTH/3046/6/18 on 17 January the Appeal Board noted that although the whole project (Phases 1-3) included features of joint working the protocol of agreement between the four companies and the NHS region was limited to completing Phase 1. The outcomes of Phase 1 were data centred rather than patient centred. The Appeal Board considered that the arrangements at Phase 1 of the project in relation to the NHS region were not a joint working project and thus no executive summary of the written agreement needed to have been published before the arrangements were implemented. The Appeal Board ruled no breaches of Clauses 20 and 9.1.

After the consideration of the appeals by AstraZeneca and Pfizer the Appeal Board agreed that Novartis and Roche should be contacted and informed of the outcome. The PMCPA Constitution and Procedure did not cover this unusual situation where more than one company was involved in the same set of circumstances and the Appeal Board had taken a different view to the Panel. Novartis and Roche were each offered the opportunity to appeal out of time. The complainant was also informed. Roche declined the opportunity to appeal. Novartis accepted the option to appeal.

**APPEAL BY NOVARTIS**

Novartis submitted that its primary argument on appeal in relation to the Panel rulings was that, whilst the ultimate expectation of the project was that the outcomes would benefit multiple stakeholders including patients, those elements of the project which Novartis actually supported (as further described below) were not patient-centred in nature, rather they were data-centred. As such, the project was not – and did not need to be - classified as joint working and no executive summary of the written agreement needed to be published.

Novartis submitted that the background to the cancer data project was set out in its response to the complaint. The project was a collaboration between a Scottish region health board and ABPI Scotland (on behalf of the four pharmaceutical companies involved; Novartis, Roche, AstraZeneca and Pfizer) that sought to drive adoption of real-world electronic health data relating to current care pathways and patient populations, and to better incorporate such data into HTA processes by developing a reproducible data-driven Scottish cancer technology evaluation framework. The overall expectation of the project (when all phases had been completed) was that the adoption of pooled real-world data would also drive a clearer understanding of the best treatment pathways in breast cancer.

Novartis submitted that the collaboration between the four companies and the NHS region was limited only to the completion of Phase 1 of a broader project which would involve three phases in total. Phase 1 of the project would be limited to the review of data related to patients' resident, diagnosed or treated within the NHS region. Phase 2 of the project would involve potentially expanding its scope to the other health boards; and Phase 3 would involve potentially expanding its scope across NHS Scotland nationally. There were no plans for the four companies to be involved in Phases 2 and 3 of the project.

**Details of the project – data-centred outcomes**

Novartis submitted that further details of the three project phases and the detail around Phase 1 of the project were set out in the project protocol. The project protocol was clear that Phase 1 of the project was strictly focused on data-centred rather than patient-centred outcomes. The project involved the development of a breast cancer data framework. The project outcomes as described in the project protocol were as follows:

1 A data dictionary – describing data fields, their origins, historical lifespan, definitions and coding.
2 A data quality report – describing missing data rates, discrepancies between alternative data sources for variables and actions needed for improvement.
3 Example epidemiological, clinical pathway and outcomes reports.

Novartis submitted that the multitude of available datasets upon which the project would be based, both within Edinburgh and nationally within Scotland, were set out in Appendix 1 to the project protocol. The required data fell broadly into four categories: patient characteristics, clinical pathway descriptors, outcome data, and resource use and healthcare burden. Furthermore, the project work plan as set out in the project protocol involved three milestones, namely:

> *Milestone 1 (months 1-12):* Create a technical data dictionary, listing fields contained within each dataset, their definitions, coding, geographical and historical remit. Obtain permissions for milestone 3.
>
> *Milestone 2 (months 1-12):* Create a technical data quality report, including missing data rates, field and coding discrepancies, between-dataset duplication and variation over time and by geographical remit. Limited reporting of population summary statistics. Map data fields to parallel fields reported from other Scottish regional and national datasets.
>
> *Milestone 3 (months 13-18):* Examples for study, reporting on clinical characteristics, patient pathways, outcomes and healthcare resource utilization. The results would be published in an end of milestone report using anonymized and aggregated data and would be used to validate the robustness of the data framework. The report would be made publicly available.

Novartis submitted that the NHS region would use the project and constituent examples to develop and refine a process for analytical specification and information gathering by external parties in order to better inform national regulatory submission. The four companies taking part in the project would then be given the opportunity to pilot this new process.

Novartis submitted that the benefits listed in the project protocol and the milestones in the project work plan were not primarily patient-focused and for the benefit of patients, rather they were data-focused and primarily for the benefit of the NHS and the pharmaceutical industry. The payments per milestone also conveyed the very data focused nature of the work being performed by those involved in the project.

**Categorisation of the project**

Novartis submitted that the project was a joint industry and NHS collaboration and the whole project included some features of joint working. However, the project outcomes were not focused on patients, but rather on helping the NHS to develop a breast cancer data framework whilst also helping the four pharmaceutical companies to explore the potential for the framework to help HTA research. This data-centred rather than patient-centred approach to the project outcomes took the project outside the scope of joint working arrangements covered by Clause 20 of the Code.

Novartis submitted that in line with the requirements of Clause 21 which gave direction on how to manage 'other funding by the company not otherwise covered by the Code', a letter of agreement dated 21 November 2017 was signed by Novartis and the ABPI. This letter of agreement also set out other terms relating to the provision of funding to ABPI by Novartis, including the basis upon which ABPI was entering into the agreement with the NHS region.

Novartis submitted that for the reasons described above, the project was purposefully not set up as a joint working arrangement. The project was however fully reviewed and approved internally by Novartis, which included involvement from Novartis medical, compliance and legal functions. The project protocol was certified on Novartis' Zinc approval system. Novartis did not have a Zinc job category to cover collaborative projects entered into by ABPI (towards which it provided funding). It was therefore decided that a 'joint working' Zinc job category should be used solely for internal approval purposes as this was the closest 'fit' to the collaborative and non-promotional nature of the project. However, it was clearly stated in the job summary within Zinc that this project was an ABPI Collaboration Agreement and not joint working. An Executive summary was not published on the Novartis website as this was an ABPI-contracted project that had not been classified externally as joint working.

Novartis submitted that joint working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experiences and/or resources for the joint development and implementation of patient-centred projects and share a commitment to successful delivery. This definition was reproduced in the supplementary information to Clause 20 Joint Working in the Code. The relevant supplementary information to Clause 20 then described the features of joint working including that it must be for the benefit of patients, but it was expected that the arrangements would also benefit the NHS

and the pharmaceutical company or companies involved. Clause 20 also required a formal written agreement to be in place and an executive summary of the joint working agreement to be made publicly available before arrangements were implemented.

Novartis noted that the Panel stated that 'To determine whether an arrangement was joint working one had to consider whether the project was for the benefit of patients. The Panel noted the benefits for all stakeholders listed in the protocol and considered that these were primarily although not exclusively for the benefit of patients' and the Panel concluded that it considered that the benefits listed in the protocol in relation to Phase 1 of the project could be predominantly characterized as for the benefit of patients. Novartis respectfully disagreed with this assessment by the Panel.

Novartis submitted that whilst Phases 1 to 3 of the project included some features of joint working as explained above, the outcomes of Phase 1 of the project were focused on data-centred rather than patient-centred outcomes and involved the development of a breast cancer data framework. Joint working projects must have a clear focus on patient benefits. This was not the case in relation to those elements of this project supported by Novartis and the other pharmaceutical companies which were predominantly focused on the benefits to the NHS and industry through the development of the breast cancer data framework.

Novartis submitted that therefore, the project was structured not as joint working, but as a collaboration arrangement. The complainant asked why an executive summary of the project did not appear on the Novartis website. An executive summary was not published on the Novartis website because the arrangements were not joint working. Therefore, the provisions of Clause 20 of the Code relating to the publication of executive summaries of the written agreement between the parties did not apply to the four companies involved in the collaboration.

Novartis submitted that the project was fully reviewed and approved internally within Novartis and the necessary documents certified. The fact that it was not a joint working project was made clear in the Zinc job summary. On this basis, Novartis appealed the Panel ruling of a breach of Clause 20 of the Code.

Novartis submitted that its involvement in this project was reviewed and approved internally in accordance with the Code and its SOPs, maintaining high standards throughout the design, approval and delivery of this innovative and collaborative non-promotional project. On the basis of its argument that this project did not constitute joint working because of its data-centred outcomes, breaches of Clauses 20 and 9.1 were inextricably linked, and if there was no breach of Clause 20 then there could be no argument that high standards were not maintained. Novartis, therefore, also appealed the Panel ruling of a breach of Clause 9.1 of the Code.

**COMMENTS FROM THE COMPLAINANT**

The complainant provided no comments on the appeal.

**APPEAL BOARD RULING**

In addition to the submission from Novartis the Appeal Board noted relevant elements of its rulings in its consideration of the appeals from Pfizer (Case AUTH/3045/6/18) and AstraZeneca (Case AUTH/3046/6/18).

The Appeal Board noted that the complaint highlighted the ABPI news publication and tweet about the Scottish collaboration with four of its member companies (including Novartis) in a named Scottish region cancer data project. The Appeal Board noted that the news article stated that 'A ground-breaking collaboration will use real-world data to investigate how well different cancer treatments really work, changing Scotland's approach to breast cancer research like never before.' The Appeal Board noted from the appeals by Pfizer (Case AUTH/3045/6/18) and AstraZeneca (Case AUTH/3046/6/18) that the communications should have been agreed by the companies and this had not been so. The companies had submitted that they would not have approved the ABPI press release as issued.

The Appeal Board noted that joint working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experience and/or resources for the joint development and implementation of patient centred projects and shared a commitment to successful delivery. This definition was reproduced in the supplementary information to Clause 20 Joint Working. The relevant supplementary information to Clause 20 described the features of joint working including that it must be for the benefit of patients, but it was expected that the arrangements would also benefit the NHS and the pharmaceutical company or companies involved. Clause 20 required a formal written agreement to be in place and an executive summary of the Joint Working agreement to be made publicly available before arrangements were implemented.

The Appeal Board noted the 'ABPI Joint Working A Quick Start Reference Guide for NHS and pharmaceutical industry partners' included a criteria checklist which stated *inter alia* that if the answer was no in response to any one of a list 10 questions then the project would not be a true Joint Working arrangement. The 10 questions included that 'The main benefit of the project is focused on the patient', 'There is a significant contribution of pooled resources (taking into account people, finance, equipment and time) from each of the parties involved', 'There is a shared commitment to joint development, implementation and successful delivery of a patient-centred project by all parties involved' and 'Patient outcomes of the project will be measured and documented'. The Appeal Board

noted that the guidance was not part of the Code or the supplementary information. It nonetheless provided helpful points for the companies to consider when assessing such arrangements. The relevant supplementary information noted that the ABPI Guidance referred to the requirements of the Code but went well beyond them. The 'ABPI Joint Working A Quick Start Reference Guide for NHS and pharmaceutical industry partners' was not referred to by Novartis.

The Appeal Board considered that the documents could have been better worded to more accurately reflect the arrangements and this included the information issued by the ABPI.

The Appeal Board noted that the four companies had each paid £32,480.50 and that the ABPI SCG had paid £10,000 towards the project giving a total of £139,922. The NHS had contributed £118,309.50. In the Appeal Board's view, the role of the ABPI did not preclude the arrangements being joint working. The Appeal Board noted Novartis's involvement in the steering committee was to monitor and report back on its progress.

The Appeal Board noted Novartis submission that it had the necessary documents certified using the Novartis joint working Zinc job category as it was the closest fit to the collaborative and non-promotional nature of the project. Novartis did not consider that the project was a joint working project. Novartis considered that the arrangements relating to the project were in line with the requirements of Clause 21 of the Code.

The Appeal Board noted that the whole project included features of joint working, namely, the pooling of industry and NHS resources to implement a project with outcomes listed in the protocol for the benefit of patients and the benefit of the NHS and the four companies involved including Novartis; both the Scottish region health board and the four companies including Novartis had made a significant financial contribution towards the project; and defined project outcomes were to be measured and documented.

However, the Appeal Board noted that the protocol of agreement was limited to completing Phase 1. The outcomes of Phase 1 were a data dictionary, a data quality report and example epidemiological, clinical pathway and outcomes reports that would be aggregated and anonymised and only available to the companies when they had been published by the NHS region. Although referred in the protocol, Phases 2 and 3 were not part of the current protocol of agreement and there was no agreement or obligation that the company would be involved in them.

The Appeal Board noted that Novartis in its appeal provided better and further particulars than had been provided to the Panel particularly with regards to the actual outcomes of Phase I. Pfizer (Case AUTH/3045/6/18) and AstraZeneca (Case AUTH/3046/6/18) also commented on the misleading nature of the ABPI press release at their appeals.

The Appeal Board noted that its role was solely to determine whether the activity at issue was joint working thereby triggering the requirement to publish an executive summary.

The Appeal Board noted that although the whole project (Phases 1-3) included features of joint working the protocol of agreement between the four companies and the NHS region was limited to completing Phase 1. The outcomes of Phase 1 were data centred rather than patient centred. The Appeal Board considered that the arrangements at Phase 1 of the project in relation to the NHS region were not a joint working project and thus no executive summary of the written agreement needed to have been published before the arrangements were implemented. The Appeal Board ruled no breaches of Clauses 20 and 9.1. The appeal on both points was successful.

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|---|---|
| **Complaint received** | **5 June 2018** |
| **Case completed** | **22 May 2019** |

**CASE AUTH/3044/6/18**

# ANONYMOUS v ROCHE

## Failure to publish joint working executive summary

**An anonymous, contactable complainant considered that a cancer data project, operating in a named Scottish region, appeared to be a joint working project although it had not been declared as such by the four companies involved including Roche. The complainant stated that the ABPI had, *inter alia*, published news of the collaboration. The complainant had not seen relevant details published on Roche's website, noting that an executive summary should be published before such projects start. If such details were on the website they were not visible and hence transparent – the project was not listed alongside Roche's other joint working projects.**

**The complainant acknowledged that it might be a very positive joint working project but queried whether, as long as their project was endorsed by the ABPI, member companies did not have to comply with the Code. The complainant queried whether the ABPI was leading companies to flagrantly bypass the Code.**

**The detailed response from Roche is given below.**

**The Panel noted that joint working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experience and/or resources for the joint development and implementation of patient centred projects and shared a commitment to successful delivery. The relevant supplementary information to the Code described the features of joint working including that it must be for the benefit of patients, but it was expected that the arrangements would also benefit the NHS and the pharmaceutical company or companies involved. The Code required a formal written agreement to be in place and an executive summary of the joint working agreement to be made publicly available before arrangements were implemented.**

**The first issue that the Panel had to decide was whether the arrangements referred to by the complainant constituted joint working.**

**To determine whether an arrangement was joint working one had to consider whether the project was for the benefit of patients. The Panel noted the benefits for all stakeholders listed in the protocol and considered that these were primarily, although not exclusively, for the benefit of patients. In the Panel's view, that there were ancillary benefits to pharmaceutical companies did not preclude the overall arrangements being considered a joint working project even if such benefits primarily influenced a company's decision to participate.**

**The Panel noted that Roche had not explained why the contract at issue was between the ABPI and the NHS region and not directly with the companies in question. The ABPI and the companies had discussed the classification of the project. Ultimately, and irrespective of such discussions, companies had to take responsibility for the project classification under the Code. In the Panel's view it was clear from an overall evaluation of the contract between the NHS region and the ABPI that the ABPI was contracting on behalf of the four companies and the use of a third party did not, in the Panel's view, mean that the companies could circumvent the requirements of the Code. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.**

**The Panel noted that the four companies had each paid £32,480.50 and that the ABPI Scottish Collaborations Group had paid £10,000 towards the project giving a total of £139,922. The NHS had contributed £118,309.50. The Contribution Agreement and Trade Mark Licence referred to the four companies. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.**

**The Panel noted Roche's submission that the NHS was acting as a service provider however the project included features of joint working, namely; industry and NHS resources had been pooled to implement a project for the benefit of patients; outcomes that would also benefit the NHS and the four companies involved; both the health board and the four companies had made a significant financial contribution towards the project; and defined project outcomes were to be measured and documented. However, not all of the benefits for stakeholders as set out in the protocol were for the benefit of patients. The Panel noted its comments above in this regard and considered that the benefits as listed in the protocol in relation to Phase 1 of the project could be predominantly characterized as for the benefit of patients. The Panel considered that the arrangements at Phase 1 of the project in relation to the NHS region were a joint working project and thus an executive summary of the written agreement ought to have been published before the arrangements were implemented. The Panel ruled breaches of the Code including that high standards had not been maintained. In the Panel's view the circumstances did not warrant a ruling of a breach of Clause 2 which was reserved to indicate particular disapproval of a company's activities and reserved for such use. No breach of Clause 2 was ruled.**

**The four pharmaceutical companies involved in the above project were each subject to a complaint. Novartis (Case AUTH/3043/6/18) and Roche (Case AUTH/3044/6/18) accepted the Panel's rulings**

**of breaches of the Code. AstraZeneca (Case AUTH/3046/6/18) and Pfizer (Case AUTH/3045/6/18) appealed those rulings.**

**At the appeals of Case AUTH/3045/6/18 and Case AUTH/3046/6/18 on 17 January the Appeal Board noted that although the whole project (Phases 1-3) included features of joint working the protocol of agreement between the four companies and the NHS region was limited to completing Phase 1. The outcomes of Phase 1 were data centred rather than patient centred. The Appeal Board considered that the arrangements at Phase 1 of the project in relation to the NHS region were not a joint working project and thus no executive summary of the written agreement needed to have been published before the arrangements were implemented. The Appeal Board ruled no breaches of the Code.**

**After the consideration of the appeals by AstraZeneca and Pfizer the Appeal Board agreed that Novartis and Roche should be contacted and informed of the outcome. The PMCPA Constitution and Procedure did not cover this unusual situation where more than one company was involved in the same set of circumstances and the Appeal Board had taken a different view to the Panel. Novartis and Roche were each offered the opportunity to appeal out of time. The complainant was also informed. Roche declined the opportunity to appeal. Novartis appealed and the Appeal Board subsequently ruled no breaches of the Code.**

An anonymous, contactable complainant considered that a cancer data project operating in a named Scottish region appeared to be a joint working project although it had not been declared as such by the four companies involved including Roche Products Limited.

The complaint was taken up with all four companies including Roche.

**COMPLAINT**

The complainant stated that in May 2018, the ABPI had, *inter alia*, published news of the project in question.

The complainant queried whether the project was a joint working project with the NHS. If that was the case, the complainant had not seen details published on Roche's website and noted in that regard that an executive summary should be published before such projects started. If details were on the website they were not very visible and hence transparent – the project certainly was not listed alongside Roche's other joint working projects.

The complainant noted that the news alert from the ABPI stated 'Funding of the project from the Scottish region was being matched and queried whether matched funding was one of the principles of joint working.

The complainant acknowledged that it sounded like good news and it might be a very positive joint working project but queried whether, as long as their project was endorsed by the ABPI, member companies did not have to comply with the Code.

The complainant queried whether the ABPI was leading companies to flagrantly bypass the Code.

When writing to Roche, the Authority asked it to respond in relation to the requirements of Clauses 2, 9.1 and 20.

**RESPONSE**

Roche explained that the ABPI Scotland Collaborations Group (SCG), one of three main strategic groups in ABPI Scotland, was a working group of ABPI member companies. The objective of the working group was to allow the sharing of project ideas and inputs from customers about potential projects, and if a project was accepted by members of ABPI SCG then the project could be progressed under appropriate governance. Budget was held by the ABPI not the group.

The collaborative project in question was the first project to be accepted by the ABPI SGP and it was agreed that the group would invest in it along with four companies including Roche. The project was initially proposed by a consultant physician and now operated through the ABPI in collaboration with the local cancer centre.

Because of the need to link data to health technology appraisals (HTAs) the proposal had been worked-up in conjunction with other groups in the ABPI. The project's aims and objectives were developed and agreed at a joint stakeholder workshop in January 2017. Focusing on the breast cancer patient pathway, from the point of diagnosis onwards, the objectives of the project were to:

- better define the gap between what was on offer from data and what could be delivered, with the aim of informing HTA data process for Scottish Medicine Consortium (the economic modelling)
- describe the data completeness, data quality and scope of a comprehensive linked regional cancer dataset
- build an analytical framework for the quantification of population size, population characteristics, clinical and patient outcomes, tolerability, healthcare costs and value of recently adopted new technologies for cancer.

The project would also:

- develop appropriate governance by which industry and others could apply for access to the dataset
- test the robustness and validity of the dataset.

The ABPI entered into a contract with the NHS region in March 2018. Roche reviewed the contract in December 2017.

Roche did not consider that the project was joint working covered by Clause 20 because:

- the primary benefit was to the industry in terms of insight gathering to inform future activities such as HTA submission
- the ABPI was a leading partner in the project and ABPI Scotland verified during the scoping process

that it was unable to conduct joint working
- whilst there might be a subsequent patient benefit from the project this collaboration was not focussed primarily on benefit of patients which was a key requirement for a joint working project.

In Roche's view the NHS was a service provider in the project and thus when considering applicability of the Code Roche considered that the arrangements fell under Clause 21, Relationships and Contracts with Certain Organisation which stated:

> 'Contracts between companies and institutions, organisations or associations of health professionals under which such institutions, organisations or associations provide any type of services on behalf of companies (or any other type of funding by the company not otherwise covered by the Code) are only allowed if such services (or other funding):
>
> - comply with Clause 19.1 or are provided for the purpose of supporting research
> - do not constitute an inducement to prescribe, supply, administer, recommend, buy or sell any medicine.'

In summary, Roche did not consider that the project fell under the scope of Clause 20 and therefore it denied any breach of Clauses 20, 9.1 or 2.

In response to a request for further information Roche stated that the project's aims and objectives, which had been agreed and ratified in January 2017, were as documented in the protocol for the Data Intelligence for the Value Appraisal of Personalised Healthcare Technologies for Cancer within [a named] Cancer Network (as provided). Roche's financial contribution towards the project was paid directly to the ABPI.

The Project had a Steering Committee on which the four industry collaborators plus the ABPI were represented alongside numerous other third-party organisations. They offered oversight, experiential comment and suggestions about progress with the project. The day-to-day running of the project was managed by a team comprised of employees from the NHS region in question, often with dual academic roles. This group was responsible for delivering as per the project outline and timelines as well as making final decisions on governance. Additional clinical/academic input came from senior personnel in the field of oncology across Scotland (represented by various organisations including, but not limited to the NHS region in question).

According to Roche, the aim of the project was to test the validity of the real-world dataset for a number of purposes including possible use in future health technology appraisal submissions. Some example questions to test the validity of the data for those purposes were stated in the project report, which had been drafted by the clinical lead. The Project Team would assess the robustness of the data in answering these questions. Any reporting of the outcome would be included in the final report of the Project Team and conclusions of the project. This would be of a reporting level suitable for the public domain. Roche had no part in delivering this work by the project team and would only see the results when compiled for publication. As a member of the Steering Group, Roche would be informed of progress of the work against the milestones agreed in the project plan.

**PANEL RULING**

The Panel noted that joint working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experience and/or resources for the joint development and implementation of patient centred projects and shared a commitment to successful delivery. This definition was reproduced in the supplementary information to Clause 20 Joint Working. The relevant supplementary information to Clause 20 then described the features of joint working including that it must be for the benefit of patients, but it is expected that the arrangements will also benefit the NHS and the pharmaceutical company or companies involved. Clause 20 required a formal written agreement to be in place and an executive summary of the joint working agreement to be made publicly available before arrangements were implemented.

Thus, in the Panel's view, it was clear that joint working would produce benefits to the NHS and pharmaceutical companies in addition to outcomes for the benefit of patients. That a joint working arrangement produced other benefits including in relation to a company's commercial interests would not necessarily preclude the overall arrangement being classified as a *bona fide* joint working project.

The complainant alleged that certain companies had failed to publish an executive summary of joint working arrangements. The first issue that the Panel had to decide was whether the arrangements constituted joint working.

The Panel noted that the complaint concerned four pharmaceutical companies including Roche. All four companies were members of the ABPI Scotland Collaboration Group. The Panel noted that although the complaint concerned the same project the companies gave differing accounts about some aspects of the project including its internal classification. Not all companies had provided all relevant documentation.

The Panel noted that the project protocol was set out in a document titled Data Intelligence for the Value Appraisal of Personalised Healthcare Technologies for Cancer within the [named] Scotland Cancer Network, Version 9, Date of Preparation June 2017 which was appended to the agreement between the ABPI and the Scottish health board, which was neither signed nor dated. The background section of the project protocol explained that the parties had identified a need to provide a robust and prospectively designed technology adoption and evaluation framework

to exploit rich routinely collected datasets for value assessment and evidence development in real world settings. The protocol explained that such data was needed by NHS decision makers and, *inter alia*, local service managers. It was noted that existing patient access schemes were inefficient and such data would also make possible more preferable population level schemes. It was also noted that there was potential for such data to be exploited by others including academic communities which relied on routine capture of electronic health data. The protocol explained that there was an urgent need to understand the detail of what was currently possible and what further developments needed to be undertaken. There were three geographical phases to the overall project: Phase 1 in relation to breast cancer patients and the NHS region; Phase 2 in relation to four health boards comprising the named cancer network; and Phase 3 was national in scope and broader than breast cancer and would be in collaboration with another organisation.

The project work plan including costings set out in the protocol was in relation to Phase 1 of the project only and had 3 milestones. Breast cancer data had been identified for Phase 1 of the project and hence the proposed collaboration with the NHS region health board which had a pre-existing data set. In the Panel's view the complaint was about this regional Phase 1 collaboration rather than subsequent phases of the project which were referred to but not detailed in the protocol. The funding provided was in relation to Phase 1 of the project.

In relation to the project at issue, the protocol set out benefits for stakeholders. Benefits for patients were listed first and described as 'Improved patient concordance, adherence and benefit from therapy through additional support of data to ensure optimal use of their medicines'; and 'Better information as a basis for patient specific treatment decisions'. The first two of three benefits for the NHS named health board were relevant to patients and included an audit framework as a basis for improved quality of care for breast cancer patients across south east Scotland and 'Improved capture of patient outcomes'. The four benefits to ABPI/industry were listed as 'Improved reputation by working jointly with NHS to benefit patients', 'Improved professional and transparent relationship and trust between ABPI, Industry and NHS Health Boards', 'Access to anonymized aggregated data through public domain reporting to highlight the outcomes of the project to allow greater disease understanding' and 'The optimal use of medicines in the appropriate patients which should mean better proactive treatment and management of patients'.

Four sub-project work packages were listed and included direct-from-data clinical pathway modelling for outcomes estimation in support of, *inter alia*, cost-effectiveness modelling for Scottish Medicines Consortium Submissions and local business cases and expanding beyond NHS activity into social care. It appeared, although it was not entirely clear, that the sub work packages related to Phases (work packages) 2 and 3 rather than the phase in question.

In relation to Phase 1 of the project, the Panel noted the companies' and NHS region's contribution as set out in the unexecuted contract between the NHS and the ABPI. The Panel noted the companies' ongoing role on the steering committee.

To determine whether an arrangement was joint working one had to consider whether the project was for the benefit of patients. The Panel noted the benefits for all stakeholders listed in the protocol and considered that these were primarily although not exclusively for the benefit of patients. In the Panel's view, that there were ancillary benefits to pharmaceutical companies did not preclude the overall arrangements being considered a joint working project even if such benefits primarily influenced a company's decision to participate.

The Panel noted that Roche had not explained why the contract was between the ABPI and NHS region rather than directly with the companies in question. The Panel acknowledged that there had been discussion between the ABPI and the companies about the classification of the project. Ultimately and irrespective of such discussions companies had to take responsibility for the project classification under the Code. In the Panel's view it was clear from an overall evaluation of the unexecuted contract between NHS region and the ABPI that the ABPI was contracting on behalf of the four companies and the use of a third party did not, in the Panel's view, mean that the companies could circumvent the requirements of the Code. The unexecuted contracted between the NHS and the ABPI stated at the section headed Compliance, in relation to declarations of the companies' involvement that the ABPI Scotland Collaborations Group comprised four named companies including Roche. A footnote stated that this statement would not be included in the wet copy contract signed by the ABPI and NHS region. The four companies were, however, listed alongside their financial contributions in Section 5 of an Appendix, Supporter Terms and Conditions, to that Agreement. The certified project protocol annexed to the certified Contribution Agreement and Trade Mark Licence did not name the companies in question.

The Panel noted that the four companies had each paid £32,480.50 and that the ABPI Scottish Collaborations Group had paid £10,000 towards the project giving a total of £139,922. The NHS had contributed £118,309.50. The Contribution Agreement and Trade Mark Licence referred to the four companies. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.

The Panel noted Roche's submission that the NHS was acting as a service provider and the arrangements for the project fell under Clause 21. The Panel noted that the project included features of joint working, namely, the pooling of industry and NHS resources to implement a project for the benefit of patients; outcomes that would also benefit the NHS and the four SCG group members; both region health board and the four companies including Roche had made a significant financial contribution towards the project; and defined project

outcomes were to be measured and documented. However, not all of the benefits for stakeholders as set out in the protocol were for the benefit of patients. The Panel noted its comments above in this regard and considered that the benefits as listed in the protocol in relation to Phase 1 of the project could be predominantly characterized as for the benefit of patients. The Panel considered that the arrangements at Phase 1 of the project in relation to NHS region were a joint working project and thus an executive summary of the written agreement ought to have been published before the arrangements were implemented. The Panel ruled a breach of Clause 20 in this regard. High standards had not been maintained, a breach of Clause 9.1 was ruled. In the Panel's view the circumstances did not warrant a ruling of a breach of Clause 2 which was reserved to indicate particular disapproval of a company's activities and reserved for such use. No breach of Clause 2 was ruled.

The four pharmaceutical companies involved in the above project were each subject to a complaint. Novartis (Case AUTH/3043/6/18) and Roche (Case AUTH/3044/6/18) accepted the Panel's rulings of breaches of Clauses 20 and 9.1. AstraZeneca (Case AUTH/3046/6/18) and Pfizer (Case AUTH/3045/6/18) appealed those rulings.

At the appeals of Case AUTH/3045/6/18 and Case AUTH/3046/6/18 on 17 January the Appeal Board noted that although the whole project (Phases 1-3) included features of joint working the protocol of agreement between the four companies and the NHS region was limited to completing Phase 1. The outcomes of Phase 1 were data centred rather than patient centred. The Appeal Board considered that the arrangements at Phase 1 of the project in relation to the NHS region were not a joint working project and thus no executive summary of the written agreement needed to have been published before the arrangements were implemented. The Appeal Board ruled no breaches of Clauses 20 and 9.1.

After the consideration of the appeals by AstraZeneca and Pfizer the Appeal Board agreed that Novartis and Roche should be contacted and informed of the outcome. The PMCPA Constitution and Procedure did not cover this unusual situation where more than one company was involved in the same set of circumstances and the Appeal Board had taken a different view to the Panel. Novartis and Roche were each offered the opportunity to appeal out of time. The complainant was also informed. Roche declined the opportunity to appeal. Novartis appealed and the Appeal Board subsequently ruled no breach of Clauses 9.1 and 20.

**Complaint received** **5 June 2018**

**Case completed** **12 November 2018**

# ANONYMOUS CONTACTABLE v PFIZER

## Failure to publish joint working executive summary

**An anonymous, contactable complainant considered that a cancer data project, operating in a named Scottish region, appeared to be a joint working project although it had not been declared as such by the four companies involved including Pfizer. The complainant stated that the ABPI had, *inter alia*, published news of the collaboration. The complainant had not seen relevant details published on Pfizer's website, noting that an executive summary should be published before such projects start. If such details were on the website they were not visible and hence transparent – the project was not listed alongside Pfizer' other joint working projects.**

**The complainant acknowledged that it might be a very positive joint working project but queried whether, as long as their project was endorsed by the ABPI, member companies did not have to comply with the Code. The complainant queried whether the ABPI was leading companies to flagrantly bypass the Code.**

**The detailed response from Pfizer is given below.**

**The Panel noted that joint working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experience and/or resources for the joint development and implementation of patient centred projects and shared a commitment to successful delivery. The relevant supplementary information to the Code described the features of joint working including that it must be for the benefit of patients, but it was expected that the arrangements would also benefit the NHS and the pharmaceutical company or companies involved. The Code required a formal written agreement to be in place and an executive summary of the joint working agreement to be made publicly available before arrangements were implemented.**

**The first issue that the Panel had to decide was whether the arrangements referred to by the complainant constituted joint working.**

**To determine whether an arrangement was joint working one had to consider whether the project was for the benefit of patients. The Panel noted the benefits for all stakeholders listed in the protocol and considered that these were primarily, although not exclusively, for the benefit of patients. In the Panel's view, that there were ancillary benefits to pharmaceutical companies did not preclude the overall arrangements being considered a joint working project even if such benefits primarily influenced a company's decision to participate.**

**The Panel noted that according to Pfizer the NHS region had requested that the contract and funding for the project were managed by the ABPI on behalf of the four funding companies. Relevant email correspondence was provided. The Panel noted the sensitivities. The ABPI and the companies had discussed the classification of the project. Ultimately, and irrespective of such discussions, companies had to take responsibility for the project classification under the Code. In the Panel's view, it was clear from an overall evaluation of the contract between the NHS region and the ABPI, and between the ABPI and each individual company, that the ABPI was contracting on behalf of the four companies and the use of a third party did not, in the Panel's view, mean that the companies could circumvent the requirements of the Code. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.**

**In relation to the project at issue, its protocol set out benefits for stakeholders. Benefits for patients were listed first and described as 'Improved patient concordance, adherence and benefit from therapy through additional support of data to ensure optimal use of their medicines'; and 'Better information as a basis for patient specific treatment decisions'. The first two of three benefits for the regional NHS board were relevant to patients and included an audit framework as a basis for improved quality of care for breast cancer patients across a Scottish region and 'Improved capture of patient outcomes'. The four benefits to ABPI/industry included 'Improved reputation by working jointly with NHS to benefit patients' and 'The optimal use of medicines in the appropriate patients which should mean better proactive treatment and management of patients'.**

**The Panel noted that the four companies had each paid £32,480.50 and that the ABPI SCG had paid £10,000 towards the project giving a total of £139,922. The NHS had contributed £118,309.50. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.**

**The Panel noted Pfizer's submission that the project was a financial grant which was classified as a MEGS. It appeared to have been certified as such. The Panel further noted Pfizer's submission that its internal policy prevented it from being able to take any form of direct benefit in return for the provision of a grant. Pfizer would, therefore, not be participating in any piloting of the HTA process. Only very brief details appeared in the protocol. This did not appear to be part of Phase 1 of the project with NHS region. The project included features of joint working, namely: industry and NHS resources had been pooled to implement a project for the benefit of patients; outcomes that would also benefit the NHS and the four companies involved; both the health board and the four companies had made significant financial contributions towards**

**the project and defined project outcomes were to be measured and documented. However, not all of the benefits for stakeholders as set out in the protocol were for the benefit of patients. The Panel noted its comments above in this regard and considered that the benefits as listed in the protocol in relation to Phase 1 of the project could be predominantly characterized as for the benefit of patients. The Panel considered that the arrangements at Phase 1 of the project in relation to the NHS region were a joint working project and thus an executive summary of the written agreement ought to have been published before the arrangements were implemented. The Panel ruled breaches of the Code including that high standards had not been maintained. In the Panel's view, the circumstances did not warrant a ruling of a breach of Clause 2 which was reserved to indicate particular disapproval of a company's activities and reserved for such use. No breach of Clause 2 was ruled. This ruling was not appealed.**

**Upon appeal by Pfizer the Appeal Board considered that the documents could have been better worded to more accurately reflect the arrangements and this included the information issued by the ABPI. The Appeal Board noted Pfizer's submission that the project was a financial grant which was classified as a MEGS. At the appeal Pfizer submitted that its position on the steering committee was good financial auditing practice to ensure that the grant was spent as agreed.**

**The Appeal Board noted that the whole project included features of joint working, namely, the pooling of industry and NHS resources to implement a project with outcomes listed in the protocol for the benefit of patients and the benefit of the NHS and the four companies involved including Pfizer; both the Scottish region health board and the four companies including Pfizer had made a significant financial contribution towards the project; and defined project outcomes were to be measured and documented. However, the Appeal Board noted that the protocol of agreement was limited to completing Phase 1. The outcomes of Phase 1 were a data dictionary, a data quality report and example epidemiological, clinical pathway and outcomes reports that would be aggregated and anonymised and only available to the companies when they had been published by the NHS region. Although referred to in the protocol, Phases 2 and 3 were not part of the current protocol of agreement and there was no agreement or obligation that the company would be involved in them.**

**The Appeal Board noted that Pfizer in its appeal provided better and further particulars than had been provided to the Panel particularly with regards to the actual outcomes of Phase I and what Pfizer considered to be the misleading nature of the ABPI press release.**

**The Appeal Board noted that its role was solely to determine whether the activity at issue was joint working thereby triggering the requirement to publish an executive summary.**

**The Appeal Board noted its comments above and considered that the benefits listed in the protocol in relation to patients would only come about if Phases 2 and 3 were undertaken and completed; there was no patient centred benefit at the end of Phase 1. The purpose of Phase 1 and its outputs were data centred rather than patient centred. The Appeal Board considered that the arrangements at Phase 1 of the project in relation to NHS region were not a joint working project and thus no executive summary of the written agreement needed to have been published before the arrangements were implemented. The Appeal Board ruled no breaches of the Code in this regard. The appeal on both points was successful.**

**Following its completion of the consideration of the appeals in Case AUTH/3045/6/18 and Case AUTH/3046/6/18 (AstraZeneca), the Appeal Board noted that the respondent companies in Case AUTH/3043/6/18 (Novartis) and Case AUTH/3044/6/18 (Roche), had accepted the Panel's rulings of breaches of the Code and had not appealed. AstraZeneca had appealed Case AUTH/3046/6/18.**

**The Appeal Board agreed that Novartis and Roche should be contacted and informed of the outcome of the appeals in Case AUTH/3045/6/18 and Case AUTH/3046/6/18. The PMCPA Constitution and Procedure did not cover this unusual situation where more than one company was involved in the same set of circumstances and the Appeal Board had taken a different view to the Panel. Novartis and Roche should each be offered the opportunity to appeal out of time and the appeal process would operate in the usual way. The complainant should also be informed. The reports for Case AUTH/3043/6/18 and Case AUTH/3044/6/18 should be updated to reflect the situation and to cross refer to the cases which were successfully appealed. Roche declined the opportunity to appeal. Novartis appealed and the Appeal Board subsequently ruled no breaches of the Code.**

An anonymous, contactable complainant considered that a cancer data project operating in a named Scottish region appeared to be a joint working project although it had not been declared as such by the four companies involved, including Pfizer.

The complaint was taken up with all four companies including Pfizer.

**COMPLAINT**

The complainant stated that in May 2018, the ABPI had, *inter alia*, published news of the project in question.

The complainant queried whether the project was a joint working project with the NHS. If that was the case, the complainant had not seen details published on Pfizer's' website, noting that an executive summary should be published before such projects started. If details were on the website they were not very visible and hence transparent – the project certainly was not listed alongside Pfizer's other joint working projects.

The complainant noted that the ABPI news alert stated that funding of the project from the region was being matched and queried whether matched funding was one of the principles of joint working.

The complainant acknowledged that it sounded like good news and it might be a very positive joint working project but queried whether, as long as their project was endorsed by the ABPI, member companies did not have to comply with the Code. The complainant queried whether the ABPI was leading companies to flagrantly bypass the Code.

When writing to Pfizer, the Authority asked it to consider the requirements of Clauses 2, 9.1 and 20.

**RESPONSE**

Pfizer stated that the project had not been set up as a joint working project and was therefore not subject to the requirements of Clause 20. The collaborative project had been designed to explore how comprehensive linked local, regional and national cancer datasets could be used to facilitate treatment decisions and deliver better outcomes and experiences for patients in Scotland. Pfizer did not consider that the project proposal met the criteria for a joint working initiative:

- The support requested from Pfizer was funding rather than pooling of skills and resources to enable delivery of the project and
- Whilst the overarching aim of the project was to better use Scottish cancer patient data to optimise patient care, a direct measurable benefit for patients would not be delivered during the execution of the project.

For these reasons Pfizer elected to support the project by provision of a financial grant towards the costs of the project in line with the requirements of Clause 19.2.

The arrangements for the Medical and Educational Goods and Services (MEGS) Grant were:

- The ABPI coordinated funding for the project on behalf of four member companies of the ABPI Scotland Collaborations Group (SCG). The total amount of funding to be provided to the NHS region was made up of contributions of £32,480.50 from each of the four companies, plus a payment of £10,000 from member company subscriptions to the ABPI SCG, held by the ABPI. The ABPI made an upfront payment of £123,681.75 on 20 April 2018, the project initiation date, and a second payment of £16,240.25 was due to be made 12 months later (documents concerning the arrangements were provided).

- At the NHS region's request the contract and funding for the project was managed by the ABPI on behalf of the four funding member companies.

- A letter of agreement between Pfizer and the ABPI set out the arrangements with respect to funding of the project. This agreement included the following provisions:
  - The ABPI must enter into a contract with the NHS region with respect to the arrangements for the project and associated funding declarations.
  - It was acknowledged that the funding was not provided to the ABPI or the NHS region to induce, influence or reward any actions.
  - The ABPI consented to relevant disclosures being made against the ABPI if applicable.
  - The ABPI and Pfizer should comply with applicable laws, regulations and industry Codes in relation to the funding.

- The ABPI then put an agreement in place with the NHS region with respect to the project activities and declarations and disclosures of funding. This agreement contained the following provisions:
  - As required by Clause 19.2, the parties acknowledged that funding was not provided to influence prescribing or purchasing decisions for any medicines.
  - As set out in the supplementary information to Clause 19.2, the contracting parties acknowledged the disclosure requirements for the funding companies. The NHS region had agreed to provide any information which might be needed to calculate the percentage of support from the companies.
  - In line with the supplementary information to Clause 19.1, the NHS region was required to prominently display the ABPI logo and funding companies' names on all materials related to the project to make the industry's involvement in the project clear from the outset.
  - Member companies must review draft materials produced in connection with the project to ensure that funding companies' names were suitably prominent. The agreement did not give funding companies the right to review the content of materials and the agreement explicitly stated that NHS region retained full control and liability concerning the activity and all promotional and marketing activities in connection with it. The project protocol also stated that no data and analyses related to clinical outcomes would be shared with the steering committee until it had been published and made publicly accessible.
  - Each member company would have the right to nominate an employee to represent it on the project steering committee which would monitor implementation of milestones, approve release of the milestone payment and potentially support the development of sub-study work packages

- These agreements had been non-promotionally certified by Pfizer in line with paragraph 8 of the supplementary information of Clause 19.1 and Clause 14.3.

- Pfizer was currently processing a payment of £32,480.50 to the ABPI, which was the company's contribution to the costs of the project. In line with the supplementary information Clause 19.2, Pfizer intended to disclose this transfer of value to the NHS region in its 2018 disclosure data.

Pfizer stated that as described above and in the enclosures, the arrangements for it to support the cancer data project complied with Clause 19. The arrangements were therefore not within scope of Clause 20 and Pfizer did not believe that any aspect of the arrangements represented a breach of that clause. The grant had been appropriately documented and kept on record by Pfizer; Pfizer submitted that it had maintained high standards in all aspects of its support for the project and had not brought discredit upon or reduced confidence in the industry. Pfizer thus strongly refuted any allegation of breaches of Clause 9.1 or Clause 2.

In response to a request for further information Pfizer submitted that it understood the meeting held on 31 January 2017 to be an exploratory meeting designed to enable the NHS region colleagues to present their project to key stakeholders and potential supporters and enable members of the ABPI SCG to determine their interest in supporting the project. The meeting invitation clearly stated that attendance at the meeting did not represent commitment to support the project. Therefore whilst the meeting minutes recorded agreement of the proposed aims and objectives of the project, this was in the context of early preliminary discussions not limited to the eventual funding companies.

At the meeting a consultant physician presented an overview of the project identifying three key aims to be addressed by linking cancer datasets. Could comprehensive linked local, regional and national cancer datasets be used to:

- understand the epidemiology of a tumour specific group to support health technology assessment (HTA)?
- facilitate the assessment of outcomes including effectiveness, tolerability and value of recently adopted new technologies for cancer?
- support improvement in patients' experience through medicines optimisation?

Two objectives were also identified for the project that would support the aims described above:

- to describe the data completeness, data quality and scope of a comprehensive linked regional cancer dataset.
- to build an analytics framework for the quantification of population size, population characteristics, clinical and patient outcomes, tolerability, healthcare costs and value of recently adopted new technologies for cancer.

The minutes of the meeting reflected that the attendees agreed that the scope of the project was of general interest and suggestions for refinement of the project protocol were also minuted.

Companies took an action from the meeting to confirm their interest in supporting the project. Pfizer assessed the project as having clear patient and NHS benefit through the potential for the NHS to better assess the outcomes associated with the introduction of new technologies for cancer as well as improved patient experience through medicines optimisation.

The potential for companies to access the linked datasets to support HTA was also of interest to Pfizer; however, it understood this potential benefit not to be limited just to the funding companies but that, if the project was successful, any company would be able to commission analyses of the linked cancer datasets. Given these aims and objectives along with the NHS region's request for financial support, rather than colleague resource, Pfizer determined that the project should be supported following the framework set out in Clause 19.

Pfizer submitted that as a funder of the project it had a very limited role on the project steering committee. Under the terms of the agreement put in place between the ABPI and the NHS region, each member company had the right to nominate an employee to represent them on the project steering committee which would monitor implementation of milestones, approve release of the milestone payment and potentially support the development of sub-study work packages. Pfizer noted that it would consider any potential sub-study work package developing from the project as a separate activity and would assess whether and/or how to support, based on the details of the work package and any associated request from the NHS region.

Pfizer's nominated representative on the project steering committee was invited to a project kick off meeting on 20 March 2018 but he/she was unable to attend. A second Pfizer representative did attend in place of the first representative. The meeting minutes summarised the topics discussed at the meeting and included the following sessions:

- Presentation of the overarching aims, objectives and deliverables of the project-consultant physician the NHS region.

- NHS region presentation of a summary of the Information Governance workstream. This presentation included a request for the four ABPI member companies supporting the project to provide advice on the potential data requirements that pharmaceutical companies would have of the comprehensive linked regional cancer dataset to support HTA applications in the future. Any advice provided by the four ABPI member companies would be used by the project governance workstream to develop a robust and appropriate information governance framework for the project. Pfizer's understanding of this request is that the information to be provided by the companies would be representative of the pharmaceutical industry's requirements as a whole and not specific to any individual companies' medicines or requirements. Although an action to provide this feedback was minuted at the kick off meeting on 20 March 2018, to date Pfizer had not provided any feedback of this nature to the project group.

- Agreement that the steering committee would meet face-to-face at months 12 and 18 of the project. This was designed to align with the project reporting milestones and in particular would enable review of the project's progress at

the 12 month point in order for the ABPI member companies to authorise release of the second tranche of funding (£16,240.25), if appropriate. Interim tele/video-conferencing steering group meetings had been agreed in order to continue to monitor progress against the project timeline.

- A communications framework for the project was discussed and the need for any proposed publications or outputs from the project to be reviewed by the ABPI member companies was reiterated. This was consistent with the Contribution Agreement and Trade Mark Licence which stated that member companies must review draft materials were produced in connection with the project to ensure that funding companies' names were suitably prominent.

An interim steering committee teleconference was held on the 2 July 2018. Pfizer's steering committee member was unavailable to attend and his/her nominated delegate failed to join the meeting due to connectivity problems. The minutes of the meeting indicated that a general progress update was provided to the group.

Pfizer submitted that this was the total extent of its ongoing involvement with the project.

Pfizer submitted that although the contract set out that the ABPI member companies supporting the project would have an opportunity to pilot the new process, Pfizer would not take up this opportunity. Pfizer's internal policy on provision of Medical and Educational Goods and Services (MEGS) prevented Pfizer being able to take any form of direct benefit in return for the provision of a grant. Pfizer suggested that each of the four member companies individually contract directly with the NHS region so that each company could address its own policy requirements within its contract, however, the NHS region requested that the contract and funding for this project be managed by the ABPI on behalf of the four funding member companies. As the member companies supporting the project had differing polices governing whether they were able to participate in piloting the process, the provision remained in the agreement but was not an opportunity that Pfizer would be able to progress.

**PANEL RULING**

The Panel noted that joint working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experience and/or resources for the joint development and implementation of patient centred projects and shared a commitment to successful delivery. This definition was reproduced in the supplementary information to Clause 20 Joint Working. The relevant supplementary information to Clause 20 then described the features of joint working including that it must be for the benefit of patients, but it is expected that the arrangements will also benefit the NHS and the pharmaceutical company or companies involved. Clause 20 required a formal written agreement to be in place and an executive summary of the joint working agreement to be made publicly available before arrangements were implemented.
Thus, in the Panel's view, it was clear that joint working would produce benefits to the NHS and pharmaceutical companies in addition to outcomes for the benefit of patients. That a joint working arrangement produced other benefits including in relation to a company's commercial interests would not necessarily preclude the overall arrangement being classified as a *bona fide* joint working project.

The complainant alleged that certain companies had failed to publish an executive summary of joint working arrangements. The first issue that the Panel had to decide was whether the arrangements constituted joint working.

The Panel noted that the complaint concerned four pharmaceutical companies including Pfizer. All four companies were members of the ABPI Scotland Collaborations Group (SCG). The Panel noted that although the complaint concerned the same project the companies gave differing accounts about some aspects of the project including its internal classification. Not all companies had provided all relevant documentation.

The Panel noted that the project protocol was set out in a document titled Data Intelligence for the Value Appraisal of Personalised Healthcare Technologies for Cancer within the [named] cancer Network, Version 9, Date of Preparation June 2017, which was appended to the agreement between the ABPI and the Scottish health board dated 13 March 2018. The background section of the project protocol explained that the parties had identified a need to provide a robust and prospectively designed technology adoption and evaluation framework to exploit rich routinely collected datasets for value assessment and evidence development in real world settings. The protocol explained that such data was needed by NHS decision makers and, *inter alia*, local service managers. It was noted that existing patient access schemes were inefficient and such data would also make possible more preferable population level schemes. It was also noted that there was potential for such data to be exploited by others including academic communities which relied on routine capture of electronic health data. The protocol explained that there was an urgent need to understand the detail of what was currently possible and what further developments needed to be undertaken. There were three geographical phases to the overall project: Phase 1 in relation to breast cancer patients and the NHS region; Phase 2 in relation to four health boards comprising the named cancer network; and Phase 3 was national in scope and broader than breast cancer and would be in collaboration with another organisation.

The project work plan including costings set out in the protocol was in relation to Phase 1 of the project only and had 3 milestones. Breast cancer data had been identified for Phase 1 of the project and hence the proposed collaboration with the NHS region health board which had a pre-existing

data set. In the Panel's view, the complaint was about this regional Phase 1 collaboration rather than subsequent phases of the project which were referred to but not detailed in the protocol. The funding provided was in relation to Phase 1 of the project.

In relation to the project at issue, the protocol set out benefits for stakeholders. Benefits for patients were listed first and described as 'Improved patient concordance, adherence and benefit from therapy through additional support of data to ensure optimal use of their medicines'; and 'Better information as a basis for patient specific treatment decisions'. The first two of three benefits for the NHS named health board were relevant to patients and included an audit framework as a basis for improved quality of care for regional breast cancer patients and 'Improved capture of patient outcomes'. The four benefits to ABPI/industry were listed as 'Improved reputation by working jointly with NHS to benefit patients', 'Improved professional and transparent relationship and trust between ABPI, Industry and NHS Health Boards', 'Access to anonymized aggregated data through public domain reporting to highlight the outcomes of the project to allow greater disease understanding' and 'The optimal use of medicines in the appropriate patients which should mean better proactive treatment and management of patients'.

Four sub-project work packages were listed and included direct-from-data clinical pathway modelling for outcomes estimation in support of, *inter alia*, cost-effectiveness modelling for Scottish Medicines Consortium Submissions and local business cases and expanding beyond NHS activity into social care. It appeared, although it was not entirely clear, that the sub work packages related to Phases (work packages) 2 and 3 rather than the phase in question.

In relation to Phase 1 of the project, the Panel noted the companies' and the NHS region's contributions as set out in the protocol. The Panel noted the companies' ongoing role on the steering committee.

To determine whether an arrangement was joint working one had to consider whether the project was for the benefit of patients. The Panel noted the benefits for all stakeholders listed in the protocol and considered that these were primarily although not exclusively for the benefit of patients. In the Panel's view, that there were ancillary benefits to pharmaceutical companies did not preclude the overall arrangements being considered a joint working project even if such benefits primarily influenced a company's decision to participate.

The Panel noted that according to Pfizer the NHS region had requested that the contract and funding for the project were managed by the ABPI on behalf of the four funding companies. Relevant email correspondence was provided. The Panel noted the sensitivities. The Panel noted that there had been discussion between the ABPI and the companies about the classification of the project. Ultimately and irrespective of such discussions companies had to take responsibility for the project classification under the Code. In the Panel's view, it was clear from an overall evaluation of the contract between the NHS region and the ABPI, and between the ABPI and each individual company, that the ABPI was contracting on behalf of the four companies and the use of a third party did not, in the Panel's view, mean that the companies could circumvent the requirements of the Code. The agreement between the ABPI and the NHS region dated 13 March stated at the section headed Compliance in relation to declaration of the companies' involvement in the project that ABPI SCG comprised four named companies including Pfizer. The four companies were also listed alongside their financial contributions in an appendix to that agreement. The project protocol appended to the agreement did not name the companies.

The Panel noted that the four companies had each paid £32,480.50 and that the ABPI SCG had paid £10,000 towards the project giving a total of £139,922. The NHS had contributed £118,309.50. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.

The Panel noted Pfizer's submission that the project was a financial grant which was classified as a MEGS. It appeared to have been certified as such. The Panel further noted Pfizer's submission that its internal policy prevented it from being able to take any form of direct benefit in return for the provision of a grant. Pfizer would, therefore, not be participating in any piloting of the HTA process. Only very brief details appeared in the protocol. This did not appear to be part of Phase 1 of the project with NHS region. The Panel noted that the project included features of joint working, namely: the pooling of industry and NHS resources to implement a project for the benefit of patients; outcomes that would also benefit the NHS and the four SCG group members; both the regional health board and the four SCG companies, including Pfizer, had made a significant financial contribution towards the project and defined project outcomes were to be measured and documented. However, not all of the benefits for stakeholders as set out in the protocol were for the benefit of patients. The Panel noted its comments above in this regard and considered that the benefits as listed in the protocol in relation to Phase 1 of the project could be predominantly characterized as for the benefit of patients. The Panel considered that the arrangements at Phase 1 of the project in relation to the NHS region were a joint working project and thus an executive summary of the written agreement ought to have been published before the arrangements were implemented. The Panel ruled a breach of Clause 20 in this regard. High standards had not been maintained, a breach of Clause 9.1 was ruled. In the Panel's view, the circumstances did not warrant a ruling of a breach of Clause 2 which was reserved to indicate particular disapproval of a company's activities and reserved for such use. No breach of Clause 2 was ruled.

**APPEAL BY PFIZER**

Pfizer submitted that the project arrangements failed to meet the requirements of a Joint Working initiative and were therefore not in breach of Clauses 20 and

9.1 of the Code for the following reasons:

1 The project did not deliver a direct, tangible and measurable benefit to patients.
2 The project protocol was not jointly developed by the NHS region/named university and the ABPI SCG member companies.
3 The support provided for the project by the ABPI SCG was simply funding and did not involve significant pooling of resources for the joint implementation of the project protocol.

The details of Pfizer's assessment of the project against these criteria were set out below.

**Reasons for Appeal Point 1 Objectives and Benefits of Joint Working Projects**

Pfizer submitted the following relevant Code and ABPI Guidance on the Benefits and Objectives of Joint Working:

- Clause 20 of the Code and the ABPI Guidance Notes on Joint Working defined Joint Working as situations where, **for the benefit of patients**, the NHS and pharmaceutical industry pooled skills, experience and/or resources for the joint development and implementation of **patient centred projects** and shared a commitment to successful delivery.
- The joint working checklist published in the ABPI Quick Start Reference Guide required that **patient outcomes of the project would be measured and documented**.
- The ABPI Joint Working with the Pharmaceutical Industry, Guide and Case Studies defined joint working as having the shared aim of **achieving pre-determined improvements for patients**.
- The ABPI Guidance Notes on Joint Working also recommended that **a set of baseline measurements should be established at the outset of the project to measure the success of the project aims, particularly patient outcomes**. The guidance notes also recommended that for longer projects (>1 year) patient outcomes should be analysed at least every six months as a minimum to ensure anticipated patient benefits were being delivered. Examples of how patient outcomes of a Joint Working project might be measured were provided in the ABPI Guidance Notes and included examples such as an increase in the number of appropriately diagnosed/ treated patients or a decrease in the number of inappropriately diagnosed/treated patients as well as changes in parameters such as patient satisfaction, understanding, concordance and adherence to therapy.
- Clause 20 of the Code and the ABPI Guidance Notes both recognised that whilst a Joint Working project must be for the benefit of patients, it was expected that the arrangements would also benefit the NHS and the pharmaceutical companies involved.

**Pfizer's Interpretation of the Code and ABPI Guidance:**

Pfizer understood these definitions and guidance notes to mean that an essential and primary requirement of a Joint Working project was a direct, tangible and measurable impact on patients during the actual implementation period of the project, such that a change in a patient focused parameter could be evaluated between the beginning and end of the project. The examples provided in the ABPI Guidance Notes of how the patient outcomes of a Joint Working project might be measured underpinned this understanding. Whilst Pfizer recognised that a Joint Working project might also benefit the NHS and pharmaceutical companies it understood that there must be a primary direct benefit to patients.

**Objectives and Benefits of the cancer data project:**

Pfizer submitted that the cancer data project was a data intelligence initiative with a high level objective of harnessing the unique data opportunities in Scotland for the primary purpose of improved health technology appraisal (HTA). Patient benefits were described as subsequent to the objective of improved HTA.

Pfizer submitted that the first step in being able to use Scottish data to improve HTA was described in the project protocol as an urgent requirement to understand the detail of what was currently possible and what further developments must be undertaken to deliver on the objective. To this end the first phase of the project, supported by the ABPI SCG, was focused on the Breast Cancer Patient Pathway in a named region of Scotland. Phase 1 of the project and the subject of this complaint had the objective of:

1 Describing the data completeness, data quality and scope of a comprehensive linked regional cancer dataset.

2 Building an analytics framework for the quantification of population size, population characteristics, clinical and patient outcomes, tolerability, healthcare costs and value of recently adopted new technologies for cancer.

The protocol went on to describe the project outcomes as:

1 A data dictionary – describing data fields, their origins, historical life span, definitions and coding.

2 A data source quality report – describing missing data rates, discrepancies between alternative data sources for variables and actions needed for improvement.

3 Example epidemiological, clinical pathway and outcomes reports.

The protocol later listed the benefits for patients as being:

- improved patient concordance, adherence and benefit from therapy through additional support of data to ensure optimal use of their medicines
- better information as a basis for specific treatment decisions.

Pfizer submitted that however these benefits would only be delivered for patients if all 3 phases of the protocol were delivered and then fully implemented at a later date. The stated objectives or outcomes for Phase 1 of the protocol were not able to deliver the patient benefits described above over the 18 month timeframe of the project. The planned outcomes or deliverables for Phase 1 of the protocol were data and data-infrastructure focused with no impact on patients during this phase of the project. Whilst milestone 3 would deliver example epidemiological, clinical pathway and outcomes reports there was no plan to implement and evaluate any changes to patient care based on these reports. For these reasons Pfizer did not believe that the project met the patient benefit requirements for Joint Working as set out in Clause 20 of the Code and ABPI Guidance Notes on Joint Working. The project objectives and outcomes of Phase 1 of the protocol primarily benefited the NHS. Whilst benefits to the NHS and Industry partners were acceptable within a Joint Working arrangement the primary objective for a Joint Working arrangement must always be a direct, tangible and measurable benefit for patients.

**Reasons for Appeal Point 2 Development of Joint Working Projects**

Pfizer submitted the following relevant Code and ABPI Guidance on the Development of Joint Working:

- Clause 20 of the Code and the ABPI Guidance Notes on Joint Working defined Joint Working as situations where, for the benefit of patients, the NHS and pharmaceutical industry pooled skills, experience and/or resources **for the joint development** and implementation of patient centred projects and shared a commitment to successful delivery.

- The Joint Working checklist published in the ABPI Quick Start Reference Guide required that there was a shared commitment to **joint development**, implementation and successful delivery of a patient- centred project by all parties involved.

**Pfizer's Interpretation of the Code and ABPI Guidance:**

Pfizer understood these definitions and guidance notes to mean that a key requirement of a Joint Working project was that the NHS and industry organisations worked together to develop the project plan or protocol. This joint responsibility for the development of the project was a key differentiator between Joint Working projects and those supported by Medical and Educational Goods and Services (MEGS) grants under Clause 19 of the Code.

**Development of the cancer data project:**

Pfizer submitted that the cancer data project aims, objectives and protocol were presented by a consultant physician from a named university to interested industry parties at a meeting held on 31 January 2017. Whilst companies attending the meeting were able to make suggestions on developments to the protocol; the aims, objectives and protocol were developed by the NHS region and the named university and did not involve any input from Pfizer. This did not represent joint development of a Joint Working initiative.

**Reasons for Appeal Point 3 Pooling of Skills, Experience and/or Resources in Joint Working Projects**

Pfizer submitted the following relevant Code and ABPI Guidance on Pooling of Skills, Experience and/or Resources:

- Clause 20 of the Code and the ABPI Guidance Notes on Joint Working defined Joint working as situations where, for the benefit of patients, **the NHS and pharmaceutical industry pool skills, experience and/or resources for the joint development and implementation** of patient centred projects and share a commitment to successful delivery.

- The ABPI Guidance Notes on Joint Working stated that **there must be a 'pooling' of resources** between the pharmaceutical company or companies and the NHS organisation(s) involved. **Each party must therefore make a significant contribution to the Joint Working Project to avoid the arrangement being considered as merely a gift, benefit in kind, donation** or some other non-promotional/commercial practice. Resources might come in various forms, including people, expertise, equipment, communication channels, information technology and finance.

- The Joint Working Toolkit described Joint Working projects as being distinctly different from sponsorship. **In sponsorship arrangements pharmaceutical companies simply provided funds for a specific event or work programme.**

**Pfizer Interpretation of the Code and ABPI Guidance:**

Pfizer understood these definitions and guidance notes to mean that it was important for pharmaceutical industry involvement in Joint Working projects to be clearly differentiated from the funding and services arrangements provided to Healthcare Organisations as MEGS grants under Clause 19 of the Code. This differentiation was often achieved through the pooling of resources over and above funding. Pfizer usually expected to see Pfizer colleague resource and expertise involved in the joint development and delivery of a project, in addition to any financial support provided. On occasions where Pfizer colleague resource was not required or appropriate for the delivery of a project, Pfizer would expect to see significant Pfizer colleague involvement in the development of a project plan, in addition to provision of funding, for the project to be considered to meet the requirements for Joint Working.

**Pooling of Skills, Experience and/or Resources in the cancer data project:**

Pfizer submitted that schedule three of the project plan set out the contributions to the project from each party. This section clearly showed that the only support being provided for the project by the ABPI SCG was direct funding and that there

was no 'in-kind' ABPI SCG member resource or expertise involved in the implementation of the project. This was further evidenced by the roles and responsibilities described in the project protocol. The NHS region and the ABPI SCG were identified as the funders of the project whereas the NHS region and the named university were identified as the sponsors of the project and therefore the parties responsible for implementation of the protocol.

Pfizer submitted that although each of the ABPI SCG funding companies had a seat on the project steering committee, the responsibilities of the steering committee, in relation to Phase 1 of the project, were limited to monitoring implementation of the project milestones and authorising the milestone funding payment as appropriate. The steering committee had no role in the joint delivery of the project milestones.

Pfizer submitted that in addition to the lack of joint implementation of the protocol, it did not believe there was a balanced contribution of direct or 'in kind' resources from both parties. The breakdown of costings set out in schedule 3 indicated the total industry direct funding of £139,922 to be approximately matched by £118,309.50 of 'in kind' and direct funding from the NHS. This however included £17,082 of NHS direct funding and £48,178 of 'in kind' NHS resource for the Cross-cutting Information Governance (IG) work package. This work package was not identified as an outcome of Phase 1 of the project but was instead described as a requirement for analytical specification and information gathering by external parties to better inform national regulatory submission and therefore related to Phase 3 of the project which had a national scope and not Phase 1. If the costs of the Cross-cutting IG work package were removed from the calculations, the NHS region's actual contribution to Phase 1 of the project was £53,049.50 and did not represent true pooling of resources as was required for a Joint Working arrangement.

Pfizer submitted that it did not contribute to the development of the project protocol, that there was no ABPI SCG colleague resource involved in the delivery/implementation of the project and that there was not a balanced contribution of resources, Pfizer did not believe that the ABPI SCG input into the project met the Joint Working requirements of significant pooling of resources for joint implementation of a project. This was a situation where funding was simply being provided for the delivery of the protocol developed by the NHS region and the named university.

**Reasons for Appeal Point 4 Joint Working Checklist**

Pfizer submitted that the 'ABPI Joint Working Quick Start Reference Guide for NHS and Pharmaceutical Partners' required that potential Joint Working projects were reviewed against the Joint Working criteria checklist to ensure that the criteria for Joint Working were met. The guidance stated that if the answer to any of the red questions was no, then the project was not a true Joint Working arrangement and should not be viewed as such.
Pfizer submitted that based on the explanations provided in points 1 to 3 above, when it assessed the NHS region cancer data intelligence project against the questions on the Joint Working criteria checklist, the project failed to meet several of the criteria set out on the checklist and was therefore not considered to constitute a Joint Working arrangement.

| | NHS region cancer data intelligence project Red Questions | Yes | No |
|---|---|---|---|
| 1 | The main benefit of the project is focused on the patient | | ✔ |
| 2 | All parties acknowledge the arrangements may also benefit the NHS and pharmaceutical partners involved | ✔ | |
| 3 | Any subsequent benefits are at an organisational level and not specific to any individual | ✔ | |
| 4 | There is a significant contribution of pooled resources (taking into account people, finance, equipment and time) from each of the parties involved | | ✔ |
| 5 | There is a shared commitment to joint development, implementation and successful delivery of a patient-centred project by all parties involved | | ✔ |
| 6 | Patient outcomes of the project will be measured and documented | | ✔ |
| 7 | All partners are committed to publishing an executive summary of the Joint Working agreement | | * |
| 8 | All proposed treatments involved are in line with national guidance where such exists | | ✔** |
| 9 | All activities are to be conducted in an open and transparent manner | ✔ | |
| 10 | Exit strategy and any contingency arrangements have been agreed | | ✔ |

* Not considered or discussed
**Project designed to inform future development of national guidance rather than to implement existing national guidance

**COMMENTS FROM THE COMPLAINANT**

The complainant apologised if he/she misinterpreted or concluded anything. Deciphering the details and complexities of this project was difficult for an individual not connected with the project and with a layman scientific understanding. It was disappointing to see that Pfizer had chosen to appeal the Panel's ruling of breaches of the Code. The complainant alleged that his/her response addressed 3 key aspects of this project that set it apart from the requirements of the definition of joint working.

**1 The project did not deliver a direct, tangible and measurable benefit to patients:**

The complainant stated that he/she was unclear why Pfizer submitted that a project must have direct, tangible and measurable benefits to patients

as this statement did not exist in the Guidance document. Section 2 (Background to Joint Working) of the ABPI Guidance to Joint Working quoting from the Department of Health (DH) published its Joint Working Guidance in February 2008 stated that the NHS perspective was 'We will involve the industry systematically to support better forward planning and to develop ways of measuring the uptake of clinically and cost effective medicines once introduced'. It also stated later in this section 'However, for Joint Working to be sustainable in the longer term, it should also bring benefits to both the NHS organisation and the pharmaceutical industry partner, such as cost effective use of NHS resources and increase in shareholder value respectively'. Therefore, it made clear that projects could be those which look to better support planning activities and ones that were looking at measurements ie be long-term in their aims.

The complainant alleged that whilst industry and the NHS could enter into business to business arrangements which should have a protocol attached to the contract quite clearly laying out the schedule of the activity and also what was being supported by the money.

The complainant alleged that a Joint Working project must be focused on benefits to patients however he/she did not accept that there was a need for this exclusively be projects which had direct, tangible and measurable benefits to patients. Furthermore, Pfizer was currently involved in such a joint working project documented on its website. For this project Pfizer cited patient benefits as below which the complainant did not see as being 'direct, tangible and measurable'.

**Benefits for Patients:**

- Improved early stage education and risk awareness of disease
- Improved activation, screening and detection of underlying conditions
- Improved patient engagement, empowerment and control over their personal care journey (overall patient experience)
- Access to preventative services including health, wellness, social and mental health interventions
- Improved access to health, wellbeing and social care services, leading to increased speed of service attainment and easier navigation of a 'one-stop shop environment', that might improve attendance and convenience for patients, their care givers and their families
- Participation in a culture of clinical research via an ethos that all patients were candidates for clinical studies
- Improved active monitoring of condition progression, management and routine check-ups to optimise clinical and or health system response
- Continual adaptation of pathways and patient interventions to balance outcome improvement with patient control over living a full and positive life with their condition.

Therefore, the complainant did not accept that this was a valid reason why Pfizer did not see this activity as a Joint Working project.

**2 The project protocol was not jointly developed by the NHS region/named university and the ABPI Scotland Collaborations Group (SCG) member companies:**

The complainant noted that Novartis in its response (Case AUTH/3043/6/18) stated that its representative on the ABPI SCG was in talks with representatives from the NHS region board during 2016. This representative brought the project to the ABPI SCG meeting. Furthermore, this person was specifically named on the protocol alongside the authors. In addition, there were further meetings where the NHS region board participants presented to and discussed the project with the ABPI SCG as documented in the enclosures from Pfizer.

The complainant stated that all it required was to meet the second key principle of joint working – that ii) there must be a 'pooling' of resources between the pharmaceutical company or companies and the NHS organisation(s) involved. Each party must, therefore, make a significant contribution to the Joint Working project to avoid the arrangement being construed as merely a gift, benefit in kind, donation or some other nonpromotional/commercial practice. Resources might come in various forms, including people, expertise, equipment, communication channels, information technology, and finance.

The complainant stated that in this case the NHS region board contribution was the data and the expertise and the pharmaceutical companies' contribution was mainly financial. The complainant therefore did not accept Pfizer's statement and refuted that there was anything in the ABPI Guidance Notes on Joint Working which required that a joint working project must be jointly developed.

**3 The support provided for the project by the ABPI SCG was simply funding and did not involve significant pooling of resources for the joint implementation of the project protocol.**

The complainant noted no statements which precluded consideration of an activity as a Joint Working project if the pharmaceutical company provided funding alone. Nevertheless, the complainant noted that:

i) Novartis' representative had been in discussion with the NHS region board since 2016 and was named on the protocol. The ABPI SCG entering into a project was jointly responsible or accountable for the activities of any of the other partnering companies.
ii) At the meeting on 31 Jan 2017 one of the objectives of this meeting was stated as 'Group Discussion to agree protocol and outcome measures with timelines – All'.
iii) In the more detailed elements of the detailed minutes and actions from meeting 31 January 2017 it was outlined that amendments to

the project initiation document (PID) was undertaken by three individuals including a Novartis representative. There were additional statements building additional activity into the proposal 'to inform a process of engagement of the NHS region with the pharma industry to access the results of analyses of healthcare data to better inform NHS regulatory submissions in the future. To support the development of these recommendations the project participating pharmaceutical companies could pilot an engagement process as part of the project and use the subsequent experience to inform the recommendations'. Additionally, the project partners were asked to submit real-world data questions that they might want answered – to be sent to the Novartis representative who would include them in the protocol.

These actions highlighted the joint development of the final protocol by the NHS and industry and also possibly for ongoing steering such that funding alone was not the sole contribution as claimed by Pfizer.

iv) The protocol had been set out covering elements of joint working – pooling of resources by the parties with funding from the companies and data and expertise from the NHS, benefits outlined for patients, industry and NHS – therefore it appeared that the NHS and the Novartis representative set out their proposal as per Joint Working.

v) The Joint Working governance (section 6 of the ABPI Guidance notes to Joint Working) advised that governance included 'entering into appropriate Joint Working agreements, establishing steering groups and consulting with relevant stakeholders about each particular Joint Working project'. In this case there was a steering group and industry and NHS representatives on the steering committee. At the meeting on 31 January 2017 one of the statements was 'Next Steps -NHS/ABPI approval process and timelines, project governance, proposed membership of the steering committee with one representative from industry, the NHS [region], NHS GGC [and others]'.

The complainant alleged that these were just a small number of reasons why he/she refuted Pfizer's claim that its contribution was solely financial in nature or that this was a basis for why this could not be considered Joint Working. The complainant therefore concluded that the three reasons given by Pfizer as the basis for its appeal were not warranted and should be rejected.

The complainant was unclear why the Scottish region health board sought to provide equity in the collaboration with the four companies by choosing the ABPI to act as a representative body for the companies. The complainant understood the advice given by the ABPI was that they could not enter into a Joint Working agreement. From the details gathered from the four separate company's responses it was possible to make the following observations: It was unclear why the NHS group wished to partner with ABPI Scotland (as stated in Novartis response letter - no evidence was given to support ABPI SCG meeting (9 May 2017) minutes). **It might simply have been that they anticipated complexities in trying to manage creating and signing separate contracts with each of the four companies.** However, the complainant alleged that it was up to the industry partners to explain the valid and compliant ways in which the project could be supported rather than concede and rush to support through funding through some collaborative arrangement which had no place in the Code. It might be that the four companies could have sought for the ABPI to draft a single contract for them to use or that lawyers from each company could have come together to draw up a single contract before providing this to the NHS and similarly had letters of intent (as they had with the ABPI) signing up to the single contract with the NHS.

The complainant alleged that the ABPI did not appear to be a 'supporter'; and state in the contract that it was acting on behalf of the ABPI SCG which it stated was also known as 'the Group' – it later defined this group as being made up of the 4 named company supporters each paying a fee of £32,480.50 each. However, going back to the meeting minutes highlighted earlier the ABPI SCG appeared to be many more companies (based on the company attendees and those who sent their apologies) and in addition in the Supporter Terms and Conditions Section 5 Fees – the wider ABPI SCG (around 23 pharma companies) appeared to have provided an additional separate funding of £10,000. The meeting minutes recorded: 'Suggested that SCG use some of its residual funds to plug any funding gaps, if it meant project could proceed where otherwise it might not'. Based on the terminology used in the minutes the complainant made an assumption that the companies who were members of this working group pool funding into a central pot rather than this money coming from the ABPI itself. The use of the ABPI Scotland Collaborations Group to define two separate and distinct groups within the contract was confusing.

The complainant alleged that it did not read that the complexity of the provision of £10,000 from the ABPI SCG had been considered – how would transparency of this funding be made apparent and disclosed as required under Clause 24. If, as suspected, this came from funds which had been contributed by the wider ABPI SCG group were these companies (an additional 19 other companies to the 4 participating companies of Roche, Novartis, AstraZeneca and Pfizer) also subject to a responsibility to disclose their indirect contribution to this activity? If it was ABPI funds – were these disclosed by the ABPI under Clause 24?

Finally, the complainant alleged that looking at Section 1 of the ABPI Guidance notes which stated 'The ABPI Code was sometimes interpreted differently by companies, in line with their own understanding of the Code and legal requirements and taking into account their individual company policies and procedures'. This could cause confusion, both between and within companies, and also externally when companies responded differently

to similar customer or NHS requests. Individual company governance arrangements were also likely to differ as ultimately, each company was responsible for managing its own activities' and that was certainly what appeared to have happened here – two companies having placed it under Clause 21, Pfizer under Clause 19 as a MEGS, another certifying it as Joint Working but documenting in certificate noted that it was not Joint Working but not considering any clause under which it could legitimately be placed.

The complainant alleged that as in his/her original complaint he/she did not deny that it might be a worthwhile project but it was the responsibility of the companies to comply with the ABPI Code and to ensure the correct and compliant procedures were followed and where necessary to advise NHS partners as to how something could be done compliantly.

**APPEAL BOARD RULING**

The Appeal Board noted that the complaint highlighted the ABPI news publication and tweet about the Scottish collaboration with four of its member companies (including Pfizer) in a named Scottish region cancer data project. The Appeal Board noted that the news article stated that 'A ground-breaking collaboration will use real-world data to investigate how well different cancer treatments really work, changing Scotland's approach to breast cancer research like never before.' The Appeal Board noted from the Pfizer's representatives at the appeal that the communications should have been agreed by Pfizer and this had not been so. Pfizer submitted that it would not have approved the ABPI press release as issued.

The Appeal Board noted that Joint Working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experience and/or resources for the joint development and implementation of patient centred projects and shared a commitment to successful delivery. This definition was reproduced in the supplementary information to Clause 20 Joint Working. The relevant supplementary information to Clause 20 described the features of Joint Working including that it must be for the benefit of patients, but it was expected that the arrangements would also benefit the NHS and the pharmaceutical company or companies involved. Clause 20 required a formal written agreement to be in place and an executive summary of the joint working agreement to be made publicly available before arrangements were implemented.

The Appeal Board noted the 'ABPI Joint Working A Quick Start Reference Guide for NHS and pharmaceutical industry partners' included a criteria checklist which stated, *inter alia*, that if the answer was no in response to any one of a list 10 questions then the project would not be a true Joint Working arrangement. The 10 questions included that 'The main benefit of the project is focused on the patient', 'There is a significant contribution of pooled resources (taking into account people, finance, equipment and time) from each of the parties involved', 'There is a shared commitment to joint development, implementation and successful delivery of a patient-centred project by all parties involved' and 'Patient outcomes of the project will be measured and documented'. The Appeal Board noted that the guidance was not part of the Code or the supplementary information. It nonetheless provided helpful points for the companies to consider when assessing such arrangements. The relevant supplementary information noted that the ABPI Guidance referred to the requirements of the Code but went well beyond them.

The Appeal Board considered that the documents could have been better worded to more accurately reflect the arrangements and this included the information issued by the ABPI.

The Appeal Board noted that the four companies had each paid £32,480.50 and that the ABPI SCG had paid £10,000 towards the project giving a total of £139,922. The NHS had contributed £118,309.50. In the Appeal Board's view, the role of the ABPI did not preclude the arrangements being joint working. The Appeal Board noted that Pfizer's involvement in the steering committee was to monitor progress and authorised the milestone funding payment.

The Appeal Board noted Pfizer's submission that the project was a financial grant which was classified as a MEGS. Pfizer's representatives at the appeal submitted that its position on the steering committee was good financial auditing practice to ensure that the grant was spent as agreed.

The Appeal Board noted that the whole project included features of joint working, namely, the pooling of industry and NHS resources to implement a project with outcomes listed in the protocol for the benefit of patients and the benefit of the NHS and the four companies involved including Pfizer; both the Scottish region health board and the four companies including Pfizer had made a significant financial contribution towards the project; and defined project outcomes were to be measured and documented. However, the Appeal Board noted that the protocol of agreement was limited to completing Phase 1. The outcomes of Phase 1 were a data dictionary, a data quality report and example epidemiological, clinical pathway and outcomes reports that would be aggregated and anonymised and only available to the companies when they had been published by the NHS region. Although referred to in the protocol, Phases 2 and 3 were not part of the current protocol of agreement and there was no agreement or obligation that the company would be involved in them.

The Appeal Board noted that Pfizer in its appeal provided better and further particulars than had been provided to the Panel particularly with regards to the actual outcomes of Phase I and what Pfizer considered to be the misleading nature of the ABPI press release.

The Appeal Board noted that its role was solely to determine whether the activity at issue was joint working thereby triggering the requirement to publish an executive summary.

The Appeal Board noted its comments above and considered that the benefits listed in the protocol in relation to patients and would only come about if Phases 2 and 3 were undertaken and completed; there was no patient centred benefit at the end of Phase 1. The purpose of Phase 1 and its outputs were data centred rather than patient centred. The Appeal Board considered that the arrangements at Phase 1 of the project in relation to the NHS region were not a joint working project and thus no executive summary of the written agreement needed to have been published before the arrangements were implemented. The Appeal Board ruled no breach of Clause 20 in this regard and consequently no breach of Clause 9.1 was ruled. The appeal on both points was successful.

During its consideration of this case the Appeal Board noted that the ABPI advice on joint working was last revised in 2008. In the Appeal Board's view, it would be helpful if such advice was revised. The type of project in the above case concerning data was increasing.

Following its completion of the consideration of the appeals in Case AUTH/3045/6/18 and Case noted that AUTH/3046/6/18 (AstraZeneca), the Appeal Board the respondent companies in Case AUTH/3043/6/18 (Novartis) and Case AUTH/3044/6/18 (Roche), had accepted the Panel's rulings of breaches of the Code and had not appealed. AstraZeneca had appealed Case AUTH/3046/6/18.

The Appeal Board agreed that Novartis and Roche should be contacted and informed of the outcome of the appeals in Case AUTH/3045/6/18 and Case AUTH/3046/6/18. The PMCPA Constitution and Procedure did not cover this unusual situation where more than one company was involved in the same set of circumstances and the Appeal Board had taken a different view to the Panel. Novartis and Roche should each be offered the opportunity to appeal out of time and the appeal process would operate in the usual way. The complainant should also be informed. The reports for Case AUTH/3043/6/18 and Case AUTH/3044/6/18 should be updated to reflect the situation and to cross refer to the cases which were successfully appealed. Roche declined the opportunity to appeal. Novartis appealed and the Appeal Board subsequently ruled no breach of Clauses 9.1 and 20.

| | |
|---|---|
| **Complaint received** | **5 June 2018** |
| **Case completed** | **17 January 2019** |

# ANONYMOUS CONTACTABLE v ASTRAZENECA

## Failure to publish joint working executive summary

**An anonymous, contactable complainant considered that a cancer data project, operating in a named Scottish region, appeared to be a joint working project although it had not been declared as such by the four companies involved including AstraZeneca. The complainant stated that the ABPI had, *inter alia*, published news of the collaboration. The complainant had not checked AstraZeneca's website but noted that he/she had not seen details published on the other three companies' websites. The complainant noted that an executive summary should be published before such projects start. If such details were on the websites of the other three companies, they were not visible and hence transparent – the project was not listed alongside those companies' other joint working projects.**

**The complainant acknowledged that it might be a very positive joint working project but queried whether, as long as their project was endorsed by the ABPI, member companies did not have to comply with the Code. The complainant queried whether the ABPI was leading companies to flagrantly bypass the Code.**

**The detailed response from AstraZeneca is given below.**

**The Panel noted that joint working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experience and/or resources for the joint development and implementation of patient centred projects and shared a commitment to successful delivery. The relevant supplementary information to the Code described the features of joint working including that it must be for the benefit of patients, but it was expected that the arrangements would also benefit the NHS and the pharmaceutical company or companies involved. The Code required a formal written agreement to be in place and an executive summary of the joint working agreement to be made publicly available before arrangements were implemented.**

**The first issue that the Panel had to decide was whether the arrangements referred to by the complainant constituted joint working.**

**To determine whether an arrangement was joint working one had to consider whether the project was for the benefit of patients. The Panel noted the benefits for all stakeholders listed in the protocol and considered that these were primarily, although not exclusively, for the benefit of patients. In the Panel's view, that there were ancillary benefits to pharmaceutical companies did not preclude the overall arrangements being considered a joint working project even if such benefits primarily influenced a company's decision to participate.**

**The Panel noted that AstraZeneca did not explain why the contract at issue was between the ABPI and the NHS region and not directly with the companies in question. The ABPI and the companies had discussed the classification of the project. Ultimately, and irrespective of such discussions, companies had to take responsibility for the project classification under the Code. In the Panel's view, it was clear from an overall evaluation of the contract between the NHS region and the ABPI, and between the ABPI and each individual company, that the ABPI was contracting on behalf of the four companies and the use of a third party did not, in the Panel's view, mean that the companies could circumvent the requirements of the Code. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.**

**In relation to the project at issue, its protocol set out benefits for stakeholders. Benefits for patients were listed first and described as 'Improved patient concordance, adherence and benefit from therapy through additional support of data to ensure optimal use of their medicines'; and 'Better information as a basis for patient specific treatment decisions'. The first two of three benefits for the regional NHS board were relevant to patients and included an audit framework as a basis for improved quality of care for breast cancer patients across a Scottish region and 'Improved capture of patient outcomes'. The four benefits to ABPI/industry included 'Improved reputation by working jointly with NHS to benefit patients' and 'The optimal use of medicines in the appropriate patients which should mean better proactive treatment and management of patients'.**

**The Panel noted that the four companies had each paid £32,480.50 and that the ABPI SCG had paid £10,000 towards the project giving a total of £139,922. The NHS had contributed £118,309.50. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.**

**The Panel noted AstraZeneca's submission that the project fell within the requirements of Clause 21, that it was a contract to provide funding for the purpose of supporting research. The Panel noted that the project included features of joint working, namely: industry and NHS resources had been pooled to implement a project for the benefit of patients; outcomes that would also benefit the NHS and the four companies involved; both the health board and the four companies had made significant financial contributions towards the project and defined project outcomes were to be measured and documented. However, not all of the benefits for stakeholders as set out in the protocol were for the benefit of patients. The Panel noted its comments above in this regard and considered that the benefits**

**as listed in the protocol in relation to Phase 1 of the project could be predominantly characterized as for the benefit of patients. The Panel considered that the arrangements at Phase 1 of the project in relation to the NHS region were a joint working project and thus an executive summary of the written agreement ought to have been published before the arrangements were implemented. The Panel ruled breaches of the Code including that high standards had not been maintained. These rulings were appealed by AstraZeneca. In the Panel's view, the circumstances did not warrant a ruling of a breach of Clause 2 which was reserved to indicate particular disapproval of a company's activities and reserved for such use. No breach of Clause 2 was ruled. This ruling was not appealed.**

**Upon appeal by AstraZeneca the Appeal Board considered that the documents could have been better worded to more accurately reflect the arrangements and this included the information issued by the ABPI.**

**The Appeal Board noted AstraZeneca's submission that the project fell within the requirements of Clause 21, that it was a contract to provide funding for the purpose of supporting research and queried whether that was indeed so. The Appeal Board noted that its role was solely to determine whether the activity at issue was joint working thereby triggering the requirement to publish an executive summary.**

**The Appeal Board noted that in its appeal AstraZeneca provided further and better particulars than had been provided to the Panel notably with regard to the vision for utilising the dataset resulting from Phase 1 and the potential benefit for patients, which AstraZeneca acknowledged could have been communicated better in the contract. AstraZeneca also commented on the misleading nature of the ABPI press release.**

**The Appeal Board noted that the whole project included features of joint working, namely, the pooling of industry and NHS resources to implement a project with outcomes listed in the protocol for the benefit of patients and the benefit of the NHS and the four companies involved including AstraZeneca; both the Scottish region health board and the four companies including AstraZeneca had made a significant financial contribution towards the project; and defined project outcomes were to be measured and documented. However, the Appeal Board noted that the protocol of agreement was limited to completing Phase 1. The outcomes of Phase 1 were a data dictionary, a data quality report and example epidemiological, clinical pathway and outcomes reports that would be aggregated and anonymised and only available to the companies when they had been published by the NHS region. Although referred to in the protocol, Phases 2 and 3 were not part of the current protocol of agreement and there was no agreement or obligation that the company would be involved in them.**

**The Appeal Board noted its comments above and considered that the benefits listed in the protocol in relation to patients and would only come about if Phases 2 and 3 were undertaken and completed; there was no patient centred benefit at the end of Phase 1. The purpose of Phase 1 and its outputs were data centred rather than patient centred. The Appeal Board considered that the arrangements at Phase 1 of the project in relation to NHS region were not a joint working project and thus no executive summary of the written agreement needed to have been published before the arrangements were implemented. The Appeal Board ruled no breaches of the Code in this regard. The appeal on both points was successful.**

**Following its completion of the consideration of the appeals in Case AUTH/3045/6/18 (Pfizer) and Case AUTH/3046/6/18, the Appeal Board noted that the respondent companies in Case AUTH/3043/6/18 (Novartis) and Case AUTH/3044/6/18 (Roche), had accepted the Panel's rulings of breaches of the Code and had not appealed. Pfizer had appealed Case AUTH/3045/6/18.**

**The Appeal Board agreed that Novartis and Roche should be contacted and informed of the outcome of the appeals in Case AUTH/3045/6/18 and Case AUTH/3046/6/18. The PMCPA Constitution and Procedure did not cover this unusual situation where more than one company was involved in the same set of circumstances and the Appeal Board had taken a different view to the Panel. Novartis and Roche should each be offered the opportunity to appeal out of time and the appeal process would operate in the usual way. The complainant should also be informed. The reports for Case AUTH/3043/6/18 and Case AUTH/3044/6/18 should be updated to reflect the situation and to cross refer to the cases which were successfully appealed. Roche declined the opportunity to appeal. Novartis appealed and the Appeal Board subsequently ruled no breaches of the Code.**

An anonymous, contactable complainant considered that a cancer data project operating in a named Scottish region appeared to be a joint working project although it had not been declared as such.

The complaint was taken up with all four companies including AstraZeneca.

**COMPLAINT**

The complainant stated that in May 2018, the ABPI had, *inter alia*, published news of the project in question.

The complainant queried whether the project was a joint working project with the NHS. The complainant had not checked AstraZeneca's website but noted that he/she had not seen details published on the other companies involved websites. The complainant noted that an executive summary should be published before such projects started. If details were on the websites of the other three companies, they were not very visible and hence transparent – the project certainly was not listed alongside those companies' other joint working projects.

The complainant noted that the ABPI news alert stated that funding of the project from the region was being matched and queried whether matched funding was one of the principles of joint working.

The complainant acknowledged that it sounded like good news and it might be a very positive joint working project but queried whether, as long as their project was endorsed by the ABPI, member companies did not have to comply with the Code. The complainant queried whether the ABPI was leading companies to flagrantly bypass the Code.

When writing to AstraZeneca, the Authority asked it to consider the requirements of Clauses 2, 9.1 and 20.

**RESPONSE**

AstraZeneca explained that a named health board, requested support from the ABPI Scotland Collaborations Group (SCG) to undertake a project with the overarching aim of harnessing the existing breast cancer data opportunities in Scotland. The project was set out to address high level questions such as could comprehensively linked cancer datasets be used to:

- understand the epidemiology of a tumour specific group to support HTA?

- facilitate the assessment of outcomes including effectiveness, tolerability and value of recently adopted new technologies for cancer?

- support improvement in patients' experience through medicines optimisation?

In order to achieve the desired outcomes outlined above, assessment of the breast cancer patient pathway from the point of diagnosis onwards, in a Scottish region, was necessary. This would entail:

- describing the data completeness, data quality and scope of a comprehensive linked regional cancer dataset and

- building an analytics framework for the quantification of population size, population characteristics, clinical and patient outcomes, tolerability, healthcare costs and value of recently adopted new technologies for cancer.

This project was intended to build a suitable linked data resource within NHS Scotland for breast cancer, with the objective of enabling future research. The project focused on the creation of a unified data resource, that the collaborators could independently interrogate under an appropriate regulatory and legal framework. Data exchange was outside the scope of the project.

**Confirmation that this project was not joint working**

Following a discussion at an ABPI SCG meeting, the ABPI confirmed to the SCG (19 June 2017) that the project between ABPI SCG and the NHS region was not joint working as outlined in Clause 20. AstraZeneca noted that the requirement for a published executive summary, as referred to by the complainant, was a pre-requisite of a joint working project as stated in Clause 20. Neither the ABPI nor AstraZeneca considered that the project was a joint working project thus no formal certification of an executive summary was undertaken. The ABPI stated that it could not enter into joint working projects and was satisfied that the project in question was collaborative working between ABPI SCG and the NHS region.

On that basis, the ABPI drew up a contract on behalf of stakeholders, including AstraZeneca, which was subsequently signed by the ABPI on 13 March 2018 and the NHS region health board on 20 March. The project started in March.

AstraZeneca considered that the project fell within Clause 21 (Relationships and Contracts with Certain Organisations) where funding was permitted for the purposes of supporting research; the project was intended to build a suitable database foundation within NHS Scotland for breast cancer with the aim of enabling future research to support HTA assessments.

AstraZeneca noted that it separately signed a contract with the ABPI in November 2017, in relation to the project.

The main internal project steps and any external project steps with AstraZeneca involvement were:

| **Project Timelines** | **Date** |
|---|---|
| First Discussions | October 2016 |
| Initial Scoping meeting | January 2017 |
| ABPI confirmation of project governance | May 2017 |
| AstraZeneca Contract review | June 2017 |
| AstraZeneca signed agreement with ABPI | November 2017 |
| AstraZeneca Transparency Disclosure | November 2017 |
| Contract Signed by ABPI President and the NHS region | March 2018 |

Apart from the initial attendance of the scoping meeting in January 2017 to gain clear oversight of the agreed aims of the project, there had been no other AstraZeneca involvement other than finalising the contract with the SCG and committing to the provision of funds.

AstraZeneca stated, in summary, that together with ABPI SCG, it considered that the funding provided to the NHS region towards the project at issue did not constitute joint working as outlined in Clause 20; the company thus did not consider that the activity was in breach of Clauses 20, 9.1 or 2.

AstraZeneca submitted that as the project was not assessed as joint working, formal certification of an executive summary, which was a pre-requisite of joint working, was not undertaken.

AstraZeneca queried the rationale for breaches of the above clauses of the Code, which it had been asked to consider in relation to this project when the complainant's request appeared to be for information only rather than a formal submission of a complaint.

In response to a request for further information, AstraZeneca stated that the protocol was an integral part of Schedule 2 of the contract signed between ABPI and the NHS region in March 2018. The final aims and objectives of the project were stated in the protocol. Proposed aims and objectives were discussed at a meeting in January 2017. The discussion at this meeting led to the final aims and objectives in the protocol. By way of ABPI membership, AstraZeneca had a position on the steering committee as defined in the protocol. The role of which was to monitor implementation of the milestones and support the development of sub-study work packages. Outside of the 'core work package' there was also a 'cross-cutting work package' described in the protocol. The purpose of which was to use high-level test queries on the newly formed linked data resource, to support development of a process for researchers to submit queries to be securely run on the data resource via the NHS. It was agreed that participating companies would suggest the test queries to be used. These test queries were documented in the protocol. Subsequently, participating companies would go on to work with relevant representatives of the NHS region to support the design of this process from an 'end user' perspective. This was expected to lead to a process enabling both manufacturers and researchers to submit requests in the future, to gain secure access to anonymised, aggregated analysis outputs that they could use to gain insights into real world cancer treatment and outcomes. Governance aspects of the project were reviewed by a senior compliance staff member and the proposed legal framework was discussed with legal to ensure that it was appropriate, and a decision was subsequently made to progress the necessary supporting documentation for the project through the usual company contractual processes. It was AstraZeneca's view that this project did not meet certification requirements in the Code. As outlined in its previous correspondence, AstraZeneca submitted that the project fell within the requirements of Clause 21, specifically that it was a contract to provide funding for the purpose of supporting research. There was no specific requirement in the Code for such contracts to be certified. AstraZeneca submitted that the definition of joint working under the ABPI Code was a formal agreement between one or more pharmaceutical companies and the NHS and others. The ABPI was the signatory of this contract, not AstraZeneca. AstraZeneca stated it was advised by the ABPI, following advice that it had taken, that this agreement was not joint working. AstraZeneca reiterated that the project fell within the requirements of Clause 21, specifically that it is a contract to provide funding for the purpose of supporting research.

AstraZeneca noted that the press release concerning the project was not submitted to AstraZeneca for review as per obligations set out in the contract between the ABPI and the NHS region. In AstraZeneca's view, the nature of the engagement should have been more explicit in the press release to avoid reader confusion.

**PANEL RULING**

The Panel noted that joint working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experience and/or resources for the joint development and implementation of patient centred projects and shared a commitment to successful delivery. This definition was reproduced in the supplementary information to Clause 20 Joint Working. The relevant supplementary information to Clause 20 then described the features of joint working including that it must be for the benefit of patients, but it is expected that the arrangements will also benefit the NHS and the pharmaceutical company or companies involved. Clause 20 required a formal written agreement to be in place and an executive summary of the joint working agreement to be made publicly available before arrangements were implemented.

Thus, in the Panel's view, it was clear that joint working would produce benefits to the NHS and pharmaceutical companies in addition to outcomes for the benefit of patients. That a joint working arrangement produced other benefits including in relation to a company's commercial interests would not necessarily preclude the overall arrangement being classified as a *bona fide* joint working project.

The complainant alleged that certain companies had failed to publish an executive summary of joint working arrangements. The first issue that the Panel had to decide was whether the arrangements constituted joint working.

The Panel noted that the complaint concerned four pharmaceutical companies including AstraZeneca. All four companies were members of the ABPI Scotland Collaborations Group (SCG). The Panel noted that although the complaint concerned the same project the companies gave differing accounts about some aspects of the project including its internal classification. Not all companies had provided all relevant documentation.

The Panel noted that the project protocol was set out in a document titled Data Intelligence for the Value Appraisal of Personalised Healthcare Technologies for Cancer within the [named] cancer Network, Version 9, Date of Preparation June 2017, which was appended to the agreement between the ABPI and the Scottish health board dated 13 March 2018. The background section of the project protocol explained that the parties had identified a need to provide a robust and prospectively designed technology adoption and evaluation framework to exploit rich routinely collected datasets for value assessment and evidence development in real world settings. The protocol explained that such data was needed by NHS decision makers and, *inter alia*,

local service managers. It was noted that existing patient access schemes were inefficient and such data would also make possible more preferable population level schemes. It was also noted that there was potential for such data to be exploited by others including academic communities which relied on routine capture of electronic health data. The protocol explained that there was an urgent need to understand the detail of what was currently possible and what further developments needed to be undertaken. There were three geographical phases to the overall project: Phase 1 in relation to breast cancer patients and the NHS region; Phase 2 in relation to four health boards comprising the named cancer network; and Phase 3 was national in scope and broader than breast cancer and would be in collaboration with another organisation.

The project work plan including costings set out in the protocol was in relation to Phase 1 of the project only and had 3 milestones. Breast cancer data had been identified for Phase 1 of the project and hence the proposed collaboration with the NHS region health board which had a pre-existing data set. In the Panel's view the complaint was about this regional Phase 1 collaboration rather than subsequent phases of the project which were referred to but not detailed in the protocol. The funding provided was in relation to Phase 1 of the project.

In relation to the project at issue, the protocol set out benefits for stakeholders. Benefits for patients were listed first and described as 'Improved patient concordance, adherence and benefit from therapy through additional support of data to ensure optimal use of their medicines'; and 'Better information as a basis for patient specific treatment decisions'. The first two of three benefits for the NHS named health board were relevant to patients and included an audit framework as a basis for improved quality of care for regional breast cancer patients and 'Improved capture of patient outcomes'. The four benefits to ABPI/industry were listed as 'Improved reputation by working jointly with NHS to benefit patients', 'Improved professional and transparent relationship and trust between ABPI, Industry and NHS Health Boards', 'Access to anonymized aggregated data through public domain reporting to highlight the outcomes of the project to allow greater disease understanding' and 'The optimal use of medicines in the appropriate patients which should mean better proactive treatment and management of patients'.

Four sub-project work packages were listed and included direct-from-data clinical pathway modelling for outcomes estimation in support of, *inter alia*, cost-effectiveness modelling for Scottish Medicines Consortium Submissions and local business cases and expanding beyond NHS activity into social care. It appeared, although it was not entirely clear, that the sub work packages related to Phases (work packages) 2 and 3 rather than the phase in question.

In relation to Phase 1 of the project, the Panel noted the companies' and the NHS region's contributions as set out in the protocol. The Panel noted the companies' ongoing role on the steering committee. To determine whether an arrangement was joint working one had to consider whether the project was for the benefit of patients. The Panel noted the benefits for all stakeholders listed in the protocol and considered that these were primarily although not exclusively for the benefit of patients. In the Panel's view, that there were ancillary benefits to pharmaceutical companies did not preclude the overall arrangements being considered a joint working project even if such benefits primarily influenced a company's decision to participate.

The Panel noted that AstraZeneca had not explained why the contract was between the ABPI and NHS region rather than directly with the companies in question. The Panel noted that there had been discussion between the ABPI and the companies about the classification of the project. Ultimately and irrespective of such discussions companies had to take responsibility for the project classification under the Code. In the Panel's view, it was clear from an overall evaluation of the contract between the NHS region and the ABPI, and between the ABPI and each individual company, that the ABPI was contracting on behalf of the four companies and the use of a third party did not, in the Panel's view, mean that the companies could circumvent the requirements of the Code. The agreement between the ABPI and the NHS region dated 13 March stated at the section headed Compliance in relation to declaration of the companies' involvement in the project that ABPI SCG comprised four named companies including AstraZeneca. The four companies were also listed alongside their financial contributions in an appendix to that agreement. The project protocol appended to the agreement did not name the companies.

The Panel noted that the four companies had each paid £32,480.50 and that the ABPI SCG had paid £10,000 towards the project giving a total of £139,922. The NHS had contributed £118,309.50. In the Panel's view, the role of the ABPI did not preclude the arrangements being joint working.

The Panel noted AstraZeneca's submission that the project fell within the requirements of Clause 21, that it was a contract to provide funding for the purpose of supporting research. The Panel noted that the project included features of joint working, namely: the pooling of industry and NHS resources to implement a project for the benefit of patients; outcomes that would also benefit the NHS and the four SCG group members; both the regional health board and the four SCG companies, including AstraZeneca, had made a significant financial contribution towards the project and defined project outcomes were to be measured and documented. However, not all of the benefits for stakeholders as set out in the protocol were for the benefit of patients. The Panel noted its comments above in this regard and considered that the benefits as listed in the protocol in relation to Phase 1 of the project could be predominantly characterized as for the benefit of patients. The Panel considered that the arrangements at Phase 1 of the project in relation to the NHS region were a joint working project and thus an executive summary of the written

agreement ought to have been published before the arrangements were implemented. The Panel ruled a breach of Clause 20 in this regard. High standards had not been maintained, a breach of Clause 9.1 was ruled. In the Panel's view, the circumstances did not warrant a ruling of a breach of Clause 2 which was reserved to indicate particular disapproval of a company's activities and reserved for such use. No breach of Clause 2 was ruled.

**APPEAL BY ASTRAZENECA**

AstraZeneca submitted that the Panel's ruling that the interaction between it (and other associated pharmaceutical companies), utilising the ABPI as a group representative agency, and the Scottish region health board was Joint Working was erroneous.

AstraZeneca submitted that to some extent, it was true that the scope of the project could appear to meet the definition for joint working as set out in the 2016 Code: 'Joint working is where, for the benefit of patients, one or more pharmaceutical companies and the NHS pool skills, experience and/or resources for the joint development and implementation of patient centred projects and share a commitment to successful delivery'.

However, AstraZeneca submitted that when considering the whole joint working framework definition, whilst the outputs of the project undertaken did have potential future longer term patient benefits, the delivery of the project outcomes (as outlined in the contract between the ABPI and the Scottish region health board, namely a data dictionary, a data quality report and example epidemiological, clinical pathway and outcomes reports), would not produce any immediate or direct patient benefits as the project aim was to create and validate a data framework, that could then be used for research or health technology evaluation in the future.

AstraZeneca outlined key aspects of this project below that set it apart from the requirements of the definition of joint working.

**1 Project objective and aims**

AstraZeneca submitted that the Scottish region health board were seeking funding to create a comprehensive linked cancer dataset, mapping out the patient pathway for breast cancer patients in their locality. In creating the resource, the authority envisaged the dataset being useful for third parties to answer key research questions, generate data for health technology submissions or to collaborate with NHS Scotland bodies to improve the patient experience and pathway. The NHS authority believed the dataset would allow them and other healthcare providers to gauge the impact of any interventions (including utilisation of particular medicines) on patient outcome measures. These ambitious benefits, that could in future be supported by the dataset, were not objectives of this project. To realise them would require new agreements, objectives and funding. To achieve their first aim of creating the linked dataset and mapping the patient pathway, the Scottish region health board chose to work with AstraZeneca and three other pharmaceutical companies. To provide equity in the collaboration with the companies, it chose the ABPI to act as the representative body for the companies. The contract that was signed was an agreement of funding between ABPI and the Scottish region health board to create the dataset, with the four pharmaceutical companies and ABPI providing a share of the funds. By funding the project, the companies were also allowed to attend project steering group meetings, with the primary intention of overseeing progress and to supply 'test' questions to ensure the validity of the dataset being created. The output of the test questions were not being utilised for any other purpose than assessing the ability of the dataset generated to answer questions typical of those that might be asked in future. The project group decided to focus on breast cancer and its related patient pathway in the first instance, with three planned phases of the project to map out pathways locally, regionally and nationally, with the contract in question focussed on delivering the first of these phases (the core work package).

**2 Direct benefits of the project to collaborating parties**

AstraZeneca submitted that the benefit of this project (if completed) would be the existence of a validated dataset that mapped the patient pathway for breast cancer patients in the Scottish region health board. The owner of this dataset was the NHS region. The industry partners would not have access to the dataset and would only see aggregated summary reports based on the high level test questions once they were published in the public domain. The existence of the dataset allowed both the industry and healthcare provider to consider initiatives or research ideas in the future, that might benefit patients and future collaborators however any further activities would be delivered under separate agreements. This project did not have any facet that was dependent on a particular medicine being prescribed or being placed in treatment algorithms.

**3 Reference to patient benefits in the contract**

AstraZeneca submitted that the patient benefits that potentially would be available at the end of the project were outlined in the contract. However, to realise the benefits (as stated above), further activity would be needed beyond the scope of this project.

AstraZeneca submitted that in hindsight the vision for utilising the dataset being created and potential benefits for patients should have been communicated better in the contract, as the current wording could propagate confusion to the nature of the collaboration when read by third party observers.

In summary, AstraZeneca submitted that whilst this project demonstrated certain aspects of joint working; the NHS and industry pooling financial resources, the true nature of the collaboration, objective and proposed output of the project did not meet the criteria of joint working as set out in Clause 20.

As AstraZeneca mainly envisaged utilising the data

for research purposes in the future, once the project had been completed, it was its opinion that the collaboration fell under the scope of Clause 21; (i) it was providing funds to support research, iregione a validated dataset on the Scottish region health board breast cancer patient pathway and aggregated outcomes; (ii) by providing funding for the project there was not an inducement to prescribe, supply, administer, recommend, buy or sell any medicine.

AstraZeneca also submitted that this project could not be considered to be a grant, due to the industry members being on the steering committee and hence being an integral part in delivering the activity. Neither was the collaboration a MEGS, as the output of this project did not enhance patient care, or benefit the NHS and maintain patient care, rather it provided a validated dataset and a theoretical future opportunity to improve or maintain patient care.

AstraZeneca, based on the above, refuted that there had been a breach of Clause 20 and Clause 9.1.

**COMMENTS FROM THE COMPLAINANT**

Firstly, the complainant confirmed that his/her notification to the PMCPA was indeed intended as a complaint and not to seek further information as speculated by AstraZeneca in its response.

The complainant apologised if he/she had misinterpreted or concluded anything. Deciphering the details and complexities of this project was difficult for an individual not connected with the project and with a layman scientific understanding.

The complainant was disappointed that AstraZeneca had chosen to appeal the Panel's rulings. The complainant addressed AstraZeneca's submission regarding three key aspects which set the project apart from the requirements of the definition of joint working.

**1 Project objectives and aims**

The complainant was unclear why AstraZeneca thought that a new agreement was needed – the protocol attached to the contract quite clearly laid out the schedule of the activity and also what was being supported by the money. Any new agreement would not necessarily be needed. In addition, this seemed irrelevant as it was the responsibility of the company to better understand the project from the outset and ensure any agreement put in place was appropriate. AstraZeneca also seemed to argue because the project was about creating a comprehensive cancer dataset it could not be considered a joint project. However, AstraZeneca had another joint working project registered on its website. The complainant alleged these projects both had similar objectives in setting up a database or creating a complete/robust e-registry.

The complainant noted AstraZeneca had explained that the Scottish region health board sought to provide equity in the collaboration with the four companies by choosing the ABPI to act as a representative body for the companies. The complainant understood the advice given by the ABPI was that it could not enter into a Joint Working agreement. Further detail was given in the Novartis response (Case AUTH/3043/6/18) and from the minutes of the ABPI Scotland Collaborations Group. The complainant alleged that it was unclear why the NHS group wished to partner with ABPI Scotland (as stated in Novartis response letter – no evidence was given to support ABPI SCG meeting (9 May 2017) minutes). It might simply have been that they anticipated complexities in trying to manage creating and signing four separate contracts with the companies. However, it was up to the industry partners to explain the valid and compliant ways in which the project could be supported rather than concede and rush to support through funding.

The complainant alleged that the ABPI did not appear to be a 'supporter' and stated in the contract that it was acting on behalf of the ABPI SCG which it stated was also known as 'the Group' – it later defined this group as being made up of the four named company supporters each paying a fee of £32,480.50. However, in the meeting minutes highlighted earlier, the ABPI SCG appeared to include many more companies (based on the company attendees and those who sent their apologies) and in addition in the Supporter Terms and Conditions Section 5 Fees – the wider ABPI SCG appeared to have provided an additional separate funding of £10,000. The meeting minutes stated 'Suggested that SCG use some of its residual funds to plug any funding gaps, if it meant project could proceed where otherwise it might not'. Based on the terminology used in the minutes, the complainant made an assumption that the companies which were members of this working group pooled funding into a central pot rather than this money coming from the ABPI itself. The use of the ABPI SCG to define two separate and distinct groups within the contract was confusing.

**2 Direct benefits of the project to collaborating parties**

The complainant stated that AstraZeneca appeared misguided in its interpretation of any requirement for Joint Working to have direct benefits of the project to collaborating parties – it stated that there would be a validated dataset for the Scottish region health board, that the industry partners would not have access to the data or preferential access before publication in the public domain. AstraZeneca appeared to argue that this could not be a joint working project because 'this project does not have any facet that is dependent on a particular medicine being prescribed or being placed in treatment algorithms'. The complainant did not accept this was a valid reason to appeal the Panel ruling nor that without these benefits to the industry partners it could not be joint working. Once again, the complainant referred to the 'Joint Working Project' posted on AstraZeneca's website. Furthermore, there could be broader more general benefits for industry partners which were reputational and could build on trust for the company in working with the NHS through Joint Working arrangements.

**3 Reference to patient benefits in the contract**

The complainant noted AstraZeneca's statement that there was no immediate or direct patient benefits and that this meant that it could not be considered as Joint Working Arrangements. The complainant did not believe this was a valid reason as there was no requirement for immediate or direct patient benefits in Joint Working arrangement requirements.

The complainant allowed that the Scottish region health board had laid out its protocol in a way which seemed to suggest that it might have considered the activity to be Joint Working – it had outlined the benefits to the Board, industry and to patients. Additionally, the Scottish region health board had also laid out the protocol to show the pooling of resources by highlighting what its monetary and benefit in kind contribution would be.

The complainant alleged that each of the companies appeared to have approached the defining of this activity within the ABPI Code in a different way. AstraZeneca suggested the arrangements should be considered under Clause 21 'Contracts between companies and institutions, organisations or associations of health professionals under which such institutions, organisations or associations provide any type of services on behalf of companies (or any other type of funding by the company not otherwise covered by the Code) are only allowed if such services (or other funding): - comply with Clause 19.1 or are provided for the purpose of supporting research'.

However, the complainant's understanding of this clause was that it was the institution, organisation or association which provided a service for the company – nowhere in the proposal or the contract did it suggest that the Scottish region health board was providing a service for AstraZeneca. The ABPI SCG meeting minutes provided in the Novartis submission (Case AUTH/3043/6/18) explained the background of the project was the frustration and the difficulty of accessing and utilising data and the lack of resources. It was unclear the significance of this statement in the minutes, but it did appear to hinge on a lack of resources to interrogate or manage the data that it had.

The complainant alleged that as in his/her original complaint he/she did not deny that it might be a worthwhile project, but it was the responsibility of the companies to comply with the ABPI Code and to ensure the correct and compliant procedures were followed and where necessary to advise NHS partners as to how something could be done compliantly.

**APPEAL BOARD RULING**

The Appeal Board noted that the complaint highlighted the ABPI news publication and tweet about the Scottish collaboration with four of its member companies (including AstraZeneca) in a named Scottish region cancer data project. The Appeal Board noted that the news article stated that 'A ground-breaking collaboration will use real-world data to investigate how well different cancer treatments really work, changing Scotland's approach to breast cancer research like never before.' The Appeal Board noted from the AstraZeneca representatives at the appeal that the communications should have been agreed by AstraZeneca and this had not been so. AstraZeneca submitted that it would not have approved the ABPI press release as issued.

The Appeal Board noted that Joint Working between the NHS and others and the pharmaceutical industry was defined by the Department of Health as situations where, for the benefit of patients, one or more pharmaceutical companies and the NHS pooled skills, experience and/or resources for the joint development and implementation of patient centred projects and shared a commitment to successful delivery. This definition was reproduced in the supplementary information to Clause 20 Joint Working. The relevant supplementary information to Clause 20 described the features of Joint Working including that it must be for the benefit of patients, but it was expected that the arrangements would also benefit the NHS and the pharmaceutical company or companies involved. Clause 20 required a formal written agreement to be in place and an executive summary of the joint working agreement to be made publicly available before arrangements were implemented.

The Appeal Board noted the 'ABPI Joint Working A Quick Start Reference Guide for NHS and pharmaceutical industry partners' included a criteria checklist which stated, *inter alia*, that if the answer was no in response to any one of a list 10 questions then the project would not be a true Joint Working arrangement. The 10 questions included that 'The main benefit of the project is focused on the patient', 'There is a significant contribution of pooled resources (taking into account people, finance, equipment and time) from each of the parties involved', 'There is a shared commitment to joint development, implementation and successful delivery of a patient-centred project by all parties involved' and 'Patient outcomes of the project will be measured and documented'. The Appeal Board noted that the guidance was not part of the Code or the supplementary information. It, nonetheless, provided helpful points for the companies to consider when assessing such arrangements. The relevant supplementary information noted that the ABPI Guidance referred to the requirements of the Code but went well beyond them.

The Appeal Board considered that the documents could have been better worded to more accurately reflect the arrangements and this included the information issued by the ABPI.

The Appeal Board noted that the four companies had each paid £32,480.50 and that the ABPI SCG had paid £10,000 towards the project giving a total of £139,922. The NHS had contributed £118,309.50. In the Appeal Board's view, the role of the ABPI did not preclude the arrangements being joint working. The Appeal Board noted that AstraZeneca's involvement in the steering committee was to monitor progress

and recommend five example test questions for use in validating the utility of the dataset.

The Appeal Board noted AstraZeneca's submission that the project fell within the requirements of Clause 21, that it was a contract to provide funding for the purpose of supporting research and queried whether that was indeed so. The Appeal Board noted that its role was solely to determine whether the activity at issue was joint working thereby triggering the requirement to publish an executive summary.

The Appeal Board noted that in its appeal AstraZeneca provided further and better particulars than had been provided to the Panel notably with regard to the vision for utilising the dataset resulting from Phase 1 and the potential benefit for patients, which AstraZeneca acknowledged could have been communicated better in the contract. AstraZeneca also commented on the misleading nature of the ABPI press release.

The Appeal Board noted that the whole project included features of joint working, namely, the pooling of industry and NHS resources to implement a project with outcomes listed in the protocol for the benefit of patients and the benefit of the NHS and the four companies involved including AstraZeneca; both the Scottish region health board and the four companies including AstraZeneca had made a significant financial contribution towards the project; and defined project outcomes were to be measured and documented. However, the Appeal Board noted that the protocol of agreement was limited to completing Phase 1. The outcomes of Phase 1 were a data dictionary, a data quality report and example epidemiological, clinical pathway and outcomes reports that would be aggregated and anonymised and only available to the companies when they had been published by the NHS region. Although referred to in the protocol, Phases 2 and 3 were not part of the current protocol of agreement and there was no agreement or obligation that the company would be involved in them.

The Appeal Board noted its comments above and considered that the benefits listed in the protocol in relation to patients and would only come about if Phases 2 and 3 were undertaken and completed; there was no patient centred benefit at the end of Phase 1. The purpose of Phase 1 and its outputs were data centred rather than patient centred. The Appeal Board considered that the arrangements at Phase 1 of the project in relation to the NHS region were not a joint working project and thus no executive summary of the written agreement needed to have been published before the arrangements were implemented. The Appeal Board ruled no breach of Clause 20 in this regard and consequently no breach of Clause 9.1 was ruled. The appeal on both points was successful.

During its consideration of this case the Appeal Board noted that the ABPI advice on joint working was last revised in 2008. In the Appeal Board's view, it would be helpful if such advice was revised. The type of project in the above case concerning data was increasing.

Following its completion of the consideration of the appeals in Case AUTH/3045/6/18 (Pfizer) and Case AUTH/3046/6/18, the Appeal Board noted that the respondent companies in Case AUTH/3043/6/18 (Novartis) and Case AUTH/3044/6/18 (Roche), had accepted the Panel's rulings of breaches of the Code and had not appealed. Pfizer had appealed Case AUTH/3045/6/18.

The Appeal Board agreed that Novartis and Roche should be contacted and informed of the outcome of the appeals in Case AUTH/3045/6/18 and Case AUTH/3046/6/18. The PMCPA Constitution and Procedure did not cover this unusual situation where more than one company was involved in the same set of circumstances and the Appeal Board had taken a different view to the Panel. Novartis and Roche should each be offered the opportunity to appeal out of time and the appeal process would operate in the usual way. The complainant should also be informed. The reports for Case AUTH/3043/6/18 and Case AUTH/3044/6/18 should be updated to reflect the situation and to cross refer to the cases which were successfully appealed. Roche declined the opportunity to appeal. Novartis appealed and the Appeal Board subsequently ruled no breach of Clauses 9.1 and 20.

**Complaint received** **5 June 2018**

**Case completed** **17 January 2019**

**CASE AUTH/3053/7/18**

# ANONYMOUS DOCTOR v DAIICHI-SANKYO

## Speaker travel arrangements

**An anonymous, contactable doctor complained about the travel arrangements, made by Daiichi-Sankyo, for a speaker at a meeting in June 2018.**

**Daiichi-Sankyo marketed Lixiana (edoxaban) which was indicated for the prevention of stroke and systemic embolism in high risk adults with nonvalvular atrial fibrillation (NVAF) and for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.**

**The complainant explained that the meeting was organised by a representative and the speaker, who had authored one of Daiichi-Sankyo's edoxaban clinical studies, was brought over from the US; he/she gave a good talk about anticoagulation. The complainant believed that the speaker was also speaking at other meetings for Daiichi-Sankyo and from conversations at the meeting, the complainant was surprised to learn that the speaker was travelling with his/her family.**

**The complainant noted that he/she had been told by other pharmaceutical companies that ABPI rules did not allow family members to travel with paid speakers. Daiichi-Sankyo should not have supported the speaker's family to come with him/her from the US.**

**The Panel noted that the speaker was a US based health professional contracted by Daiichi-Sankyo Europe GmbH based in Germany, to speak at a series of meetings aimed at health professionals in the Republic of Ireland and the UK. Daiichi-Sankyo UK stated that it was involved in planning discussions with its parent company and two agencies, regarding the arrangements for the speaker's meetings and travel in the UK. The Panel further noted that the speaker's expense claim was reviewed by Daiichi-Sankyo UK.**

**The Panel noted Daiichi-Sankyo's submission that the speaker's family who were travelling with him/her had not received any hospitality from Daiichi-Sankyo or its agencies. The Panel noted however, that the speaker requested that a van be booked for the transfer from the airport to the hotel because he/she was travelling from Ireland into the UK with four family members. At the instruction of Daiichi-Sankyo Europe a minivan was booked. The Panel noted Daiichi-Sankyo's submission that when the speaker claimed for expenses (including flights which he/she booked him/herself and meals) the minivan cost would be deducted and only his/her meals and flights would be reimbursed. The Panel noted that the impression given by the arrangements was important and queried why the speaker was not required to pay the minivan cost upfront as he/she had done with his/her flights and meals.**

**The Panel noted that whilst a minivan to transfer the speaker and his/her family to his/her hotel was booked and paid for by a third party on behalf of Daiichi-Sankyo, the cost of this transport was deducted from the speaker's expense claim and, therefore, no breach of the Code was ruled. This ruling was not appealed by the complainant.**

**The Panel noted that the restaurant invoices provided with the speaker's expense claim included meals for more than one person. It appeared that the speaker's individual meals and drinks had been highlighted and it was only the cost of these that were claimed for and reimbursed. The Panel noted that whilst Daiichi-Sankyo had identified and deducted two payments because the expenditure appeared to be for two or more people, it had missed a third. It appeared that the cost of all of the drinks ordered (including two cokes and two teas) at the restaurant was reimbursed to the speaker despite the receipt indicating that more than one person dined. In the Panel's view it appeared that on the balance of probabilities Daiichi-Sankyo had therefore reimbursed the speaker for hospitality for his/her family and a breach of the Code was ruled. This ruling was accepted by Daiichi-Sankyo.**

**The Panel noted that the speaker's expense claim was received and reviewed following receipt of this complaint and despite its awareness of the allegation, Daiichi-Sankyo had apparently reimbursed the speaker for hospitality for his/her family. The Panel considered that Daiichi-Sankyo had failed to maintain high standards and a breach of the Code was ruled. This ruling was accepted by Daiichi-Sankyo.**

**The Panel noted its rulings and comments above but did not consider that the particular circumstances of this case were such as to warrant a breach of Clause 2 which was a sign of particular censure. No breach of Clause 2 was ruled. This ruling was upheld on appeal by the complainant.**

An anonymous doctor complained about the travel arrangements, made by Daiichi-Sankyo, for a speaker at a meeting which took place in June 2018.

Daiichi-Sankyo marketed Lixiana (edoxaban) which was indicated for the prevention of stroke and systemic embolism in high risk adults with nonvalvular atrial fibrillation (NVAF) and for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

**COMPLAINT**

The complainant explained that the meeting was organised by a representative and the speaker, the speaker, who had authored one of Daiichi-Sankyo's edoxaban clinical studies, was brought over from the

US; he/she gave a good talk about anticoagulation. The complainant believed that the speaker was also speaking at other meetings for Daiichi-Sankyo as part of his/her travels, however, from conversations with others at the meeting, the complainant was surprised to learn that the speaker was travelling with his/her family.

The complainant noted that he/she had spoken at meetings for other pharmaceutical companies and had been categorically told that ABPI rules did not allow family members to travel with paid speakers. The complainant did not consider that Daiichi-Sankyo should have supported the speaker's family to come with him/her from the US.

The complainant subsequently submitted that the speaker was traveling with his/her family to a number of different countries to give talks for Daiichi-Sankyo. The speaker had spoken elsewhere before the meeting in question and had more presentations planned. When writing to Daiichi-Sankyo, the Authority asked it to consider the requirements of Clauses 2, 9.1, 22.1 and 23.1 of the Code.

**RESPONSE**

Daiichi-Sankyo explained that the speaker was an author of one of the studies for edoxaban. He/she was regarded as an international expert in the field and had extensive knowledge of the study.

Daiichi-Sankyo stated that its parent company, Daiichi-Sankyo Europe GmbH, was based in Munich, Germany. Daiichi-Sankyo Europe had the marketing authorisation for edoxaban and had contracted the speaker to travel from the US to speak at a series of meetings aimed at health professionals. The purpose of the meetings was to educate health professionals in order to optimise their anticoagulation management of patients. A copy of the contract was provided. Three meetings took place in the UK. The complainant had referred to the second meeting.

Daiichi-Sankyo UK stated that it was involved in planning discussions with its parent company and two agencies, regarding the arrangements for the speaker's meetings and travel in the UK. One agency had handled the logistical aspects in the UK including travel and accommodation, while the other agency facilitated the production of the slides including referencing. The medical content was developed by the speaker.

The speaker's primary contacts for liaison purposes were with Daiichi-Sankyo Europe and the second agency.

Daiichi-Sankyo UK became aware during the planning meetings that the speaker planned to travel with his/her family but it was very clear during discussions with Daiichi-Sankyo Europe, and its two agency's that hospitality could not be provided to any member of the speaker's family, as per the Code.

**Fees paid for services**

The speaker was paid by Daiichi-Sankyo Europe for 18 hours of meetings and 20 hours of preparation (total 38 hours). The 18 hours of meetings included multiple meetings held in Ireland, and three meetings held in the UK in June 2018. The 20 hours of preparation consisted of preparation of lectures (8 hours); telephone briefings and post event debrief (3 hours); on-site briefings (6 hours) and on-site consultancy with internal Daiichi-Sankyo functions (3 hours).

This fee was for the entire series of meetings held across Ireland and the UK and was detailed in the contract. Daiichi-Sankyo stated that this represented reasonable and fair market value for the services provided by the speaker, as per Clause 23.1 of the Code.

**Flights**

The speaker booked his/her own flights to and from the US, and between Ireland and the UK, and was expected to claim the costs for these back in expenses from Daiichi-Sankyo Europe. Details were given. The contract stated that the speaker would be reimbursed for his/her own business class flights. There would be no reimbursement for tickets for any family member. As the speaker booked his/her own flights, Daiichi-Sankyo would not have details of his/her flights until he/she submitted his/her expense claims. The speaker had not yet done so, but details could be provided when the claims were processed. The cost of an airport transfer (see below) would be deducted from the total expense claim.

**Airport transfers**

The speaker informed the second agency that he/she would like to have a van booked for the transfer from the airport to the hotel. This was because he/she was travelling from Ireland into the UK with four family members. The second agency informed the first agency of the request, and it was discussed with Daiichi-Sankyo Europe. It was recognised that it would not be practical for a separate vehicle to be booked for the speaker alone, while his/her family travelled in another vehicle at his/her own expense. At the instruction of Daiichi-Sankyo Europe, the first agency therefore arranged a minivan to transfer the speaker and his/her family to his/her hotel. The invoice was provided.

When the speaker submitted his/her expense claims, the cost of this airport transfer would be deducted from the payment made to him/her. Therefore, there would be no hospitality for his/her family at Daiichi-Sankyo's expense, in accordance with the supplementary information of Clause 22.1. Daiichi-Sankyo offered to forward the outcome of the expense claims when they were processed.

No return airport transfers were booked by Daiichi-Sankyo or its agencies and nor would they be reimbursed to the speaker. The speaker made his/her own way back to the US.

**Travel between hotel and meetings in UK**

A representative drove the speaker between his/her hotel and meeting venues in the UK. No member of the speaker's family accompanied him/her on these

journeys or attended the meetings, in accordance with Clause 22.1 of the Code.

**Accommodation in the UK**

The first agency booked for the speaker to stay for three nights in the UK at a 4 star hotel. The booking was for a standard double room for 1 adult, with breakfast. The booking confirmation was provided. No incidental room charges were made, and the final invoice (copy provided) for the bed and breakfast package for three nights was paid by the agency. No arrangements or payments were made by Daiichi-Sankyo or its agencies for the accommodation of any of the speaker's family members in the UK. The speaker indicated to the agency that he/she would arrange and pay for additional rooms him/herself to accommodate his/her family. The cost of any additional rooms would not be reimbursed to the speaker.

**Meals**

Aside from breakfast, which was included in his/her hotel room rate, the speaker's contract stated that he/she would be offered up to 12 meals organised by Daiichi-Sankyo Europe for the entire trip including Ireland and the UK. The speaker declined these meals in the UK. The speaker was expected to submit expense claims for meals he/she took in the UK. These costs would be reimbursed for his/her meals alone based on itemised receipts. The speaker's family's meals would not be reimbursed. As stated previously, the costs for the airport transfer minivan would be deducted from the overall expense reimbursement.

**Details of who made the travel arrangements**

In summary, the airport transfer booking from the airport to the hotel was made and paid for by the first agency, at the instruction of Daiichi-Sankyo Europe. These costs would be deducted from the overall expenses paid to the speaker.

Hotel accommodation for the speaker alone was booked and paid for by the first agency.

Travel between the meetings and the hotel was in a representative's car and the speaker was not accompanied by any family members.

Some aspects of the travel, such as flights and outgoing airport transfer leaving the UK were booked and paid for by the speaker. The flights would be reimbursed for the speaker alone with a deduction for the incoming airport transfer.

**Agenda for meeting at issue**

Daiichi-Sankyo noted that 'Save the Date' material was produced for the meeting and this also served as the agenda. A copy of the material was provided.

**Clauses of the Code**

With regard to Clause 22.1 and its supplementary information, Daiichi-Sankyo did not believe there had been a breach. Clause 22.1 supplementary information stated that 'spouses and other accompanying persons… may not attend the actual meeting and may not receive any associated hospitality at the company's expense; the entire costs which their presence involves are the responsibility of those they accompany'. The speaker's family who were travelling with him/her had not received any hospitality from Daiichi-Sankyo or its agencies. While an airport transfer was booked for practical reasons to accommodate the speaker and his/her family in the same vehicle, the costs for this would be deducted from the overall expenses that were paid to the speaker. None of the speaker's family members attended the meetings.

Daiichi-Sankyo denied a breach of Clause 23.1. Clause 23.1 allowed health professionals to act as consultants for services such as speaking. A written contract was agreed before the commencement of the services, and the compensation was reasonable and reflected the fair market value for the services provided.

Daiichi-Sankyo submitted that it had maintained high standards and had not brought discredit upon, or reduced confidence in the pharmaceutical industry so there had been no breach of Clause 9.1 or 2.

Daiichi-Sankyo noted that the arrangements for this series of meetings was approved by Daiichi-Sankyo Inc which was the Daiichi-Sankyo affiliate based in the US. The company required engagements with US health professionals to be approved at Daiichi-Sankyo Inc level, based on US regulations.

In response to a request for further information Daiichi-Sankyo submitted that Daiichi-Sankyo Europe contracted the speaker to travel from the US to speak at a series of meetings aimed at health professionals first in the Republic of Ireland and then in the UK. The purpose of the meetings was to educate health professionals in order to optimise their anticoagulation management of patients. Daiichi-Sankyo Europe reimbursed the speaker for expenses incurred.

According to Daiichi-Sankyo, the speaker originally submitted expenses which was reviewed by Daiichi-Sankyo UK. Two deductions were made because the receipts indicated that expenditure was incurred for two or more people. An additional deduction was made for airport taxi costs incurred by Daiichi-Sankyo for the speaker and members of his/her family on arrival at the airport as stated in Daiichi-Sankyo's original response. The speaker accepted the amendments in full. Details of the expense claim by item and invoices were provided.

**PANEL RULING**

The Panel noted that the Code applied to the promotion of medicines to members of the United Kingdom health professionals and to other relevant decision makers. The Panel noted that the speaker was a US based health professional that was contracted by Daiichi-Sankyo's parent company, Daiichi-Sankyo Europe GmbH based in Germany, to speak at a series of meetings aimed at health professionals in the Republic of Ireland and the UK. Daiichi-Sankyo UK stated that it was involved in

planning discussions with its parent company and two agencies, regarding the arrangements for the speaker's meetings and travel in the UK. The Panel further noted that the speaker's expense claim was reviewed by Daiichi-Sankyo UK.

The Panel further noted that the supplementary information to Clause 1.11 Applicability of Codes stated that pharmaceutical companies must ensure that they comply with all applicable codes, laws and regulations to which they are subject. This was particularly relevant when activities/materials involved more than one country or when a pharmaceutical company based in one country was involved in activities in another country. Activities carried out and materials used by a pharmaceutical company located in a European country must comply with the national code of that European country as well as the national code of the country in which the activities took place or the materials were used. Activities carried out and materials used in a European country by a pharmaceutical company located in a country other than a European country must comply with the EFPIA Code as well as the national code of the country in which the activities were carried out and materials were used.

The Panel noted the UK nexus and considered that the UK Code applied to the speaker's arrangements in the UK. The Panel noted that Daiichi-Sankyo made no submission in this regard; it had not argued that the matter was outside the scope of the Code.

The Panel noted that Clause 22.1 stated, *inter alia*, that hospitality offered in association with meetings must not extend beyond health professionals and other relevant decision makers. The supplementary information stated that spouses and other accompanying persons, unless qualified as above, may not attend the actual meeting and may not receive any associated hospitality at the company's expense; the entire costs which their presence involves were the responsibility of those they accompany.

The Panel noted Daiichi-Sankyo's submission that the speaker's family who were travelling with him/her had not received any hospitality from Daiichi-Sankyo or its agencies. The Panel noted however, that the speaker requested that a van be booked for transfer from the airport to the hotel because he/she was travelling from Ireland into the UK with four family members. At the instruction of Daiichi-Sankyo Europe a minivan to transfer the speaker and his/her family to his/her hotel was booked. The Panel noted Daiichi-Sankyo's submission that when the speaker claimed for expenses (including flights which he/she booked himself and meals) the minivan cost would be deducted and only his/her meals and flights would be reimbursed. The Panel noted that the impression given by the arrangements was important and queried why the speaker was not required to pay the minivan cost upfront as he/she had done with flights and meals.

The Panel noted that Clause 23.1, which covered the use of consultants and the criteria the arrangements for such services needed to fulfil, stated, *inter alia*, that health professionals and other relevant decision makers may be used as consultants and advisors, whether in groups or individually, for services such as speaking at and chairing meetings where such participation involves remuneration and/or travel. The Panel noted that whilst a minivan to transfer the speaker and his/her family to his/her hotel in June 2018 was booked and paid for by a third party on behalf of Daiichi-Sankyo, the cost of this transport was deducted from the speaker's expense claim and, therefore, no breach of Clause 23.1 was ruled. This ruling was not appealed by the complainant.

The Panel noted that the restaurant invoices provided with the speaker's expense claim included meals for more than one person. It appeared that the speaker's individual meals and drinks had been highlighted and it was only the cost of these that were claimed for and reimbursed. The Panel noted that whilst Daiichi-Sankyo had identified and deducted two payments because the expenditure appeared to be for two or more people, it had missed a third. It appeared that the cost of all of the drinks ordered (including two cokes and two teas) at a restaurant was reimbursed to the speaker despite the receipt indicating that more than one person dined. In the Panel's view it appeared that on the balance of probabilities Daiichi-Sankyo had therefore reimbursed the speaker for hospitality for his family and a breach of Clause 22.1 was ruled. This ruling was accepted by Daiichi-Sankyo.

The Panel noted that the speaker's expense claim was received and reviewed following receipt of this complaint and despite its awareness of the allegation, Daiichi-Sankyo had apparently reimbursed the speaker for hospitality for his/her family. The Panel considered that Daiichi-Sankyo had failed to maintain high standards and a breach of Clause 9.1 was ruled. This ruling was accepted by Daiichi-Sankyo.

The Panel noted its rulings and comments above but did not consider that the particular circumstances of this case were such as to warrant a breach of Clause 2 which was a sign of particular censure. No breach of Clause 2 was ruled. This ruling was appealed by the complainant.

**APPEAL BY THE COMPLAINANT**

The complainant stated that he/she was confused by the Panel's ruling and needed to read the clauses in more detail. At one point there was no breach of Clause 23.1 but later it stated this was 23.2. It must be Clause 23.1 as the complainant noted that he/she did not really complain about public disclosure of fees. The complainant alleged that he/she could not say much about Clause 23.1 anyway as he/she had not seen any contract or agreement. Was this withheld by the company?

The complainant alleged that there was discredit brought on the industry so he/she appealed the ruling of no breach of Clause 2. The complainant stated that he/she had been told that he/she could not bring family members to these kinds of meetings by other companies so he/she did not see why

Daiichi-Sankyo had different rules. By Daiichi-Sankyo's own admission it arranged transport for the family from the airport. Even if Daiichi-Sankyo ended up not paying for it after the expenses, it did organise and pay for it initially so surely this was hospitality? And did Daiichi-Sankyo only decide to do this after he/she complained? Did this not reduce confidence in the industry?

Clearly the speaker was dining out with his/her family as well; the complainant queried if the Appeal Board could be sure they were not included in these expenses? Already it was noted that some of their soft drinks were paid for. These might be matters of a few pounds but surely there was a principle to uphold. And how likely was it that the speaker used one hotel room paid for by the company whilst the rest of his/her family used another one, it was a double room after all?

The complainant alleged that the company had acted outside what it was allowed to do and there must be the same rules for all.

The PMCPA advised the complainant that its letter providing the outcome of the Panel's consideration contained an error. The Panel ruling in that letter correctly referred to the Panel's ruling of no breach of Clause 23.1, however, the penultimate paragraph of the letter referred, in error, to Clause 23.2 rather than Clause 23.1. The complainant was asked to clarify if he/she was appealing the Panel's ruling of no breach of Clause 23.1 and to provide any further detailed comments for appeal.

The complainant noted that he/she had read the clauses again including Clause 23.1 and could not see how this was relevant to the booking of the minivan for the family. Surely the minivan would fall under Clause 22.1 which stated that hospitality could not be provided to family members? So the complainant did not appeal the Panel's ruling of no breach of Clause 23.1, but the complainant thought this should be considered under Clause 22.1. Daiichi-Sankyo had provided drinks and the minivan to the family members. Even if Daiichi-Sankyo later recouped the cost of the van from the speaker, it should not have provided this hospitality in the first place.

The complainant noted that he/she had already given the reasons about why he/she was appealing Clause 2 above.

**COMMENTS FROM DAIICHI-SANKYO**

Daiichi-Sankyo noted that the complainant referred to the arrangements by Daiichi-Sankyo Europe of a mini-van to transport the speaker and his/her family from the airport to their hotel. However, the complainant had not appealed the Panel's rulings of no breach of Clause 23.1 in that regard, therefore Daiichi-Sankyo would not address the complainant's comments on the arrangements of the minivan in its response to this appeal.

Daiichi-Sankyo also noted that the complainant speculated about the arrangements for the speaker's accommodation. This matter had not been raised in the initial complaint and it was not a matter that the Panel had considered, therefore Daiichi-Sankyo would also not address the complainant's comments regarding this matter.

Daiichi-Sankyo fully appreciated the complainant's concerns, the supplementary information to Clause 22.1 noted that, for spouses and other persons accompanying a health professional, the entire costs which their presence involved was the responsibility of those they accompanied; the Code did not prohibit such persons to accompany a health professional. Impression was of course a factor to also consider.

Daiichi-Sankyo submitted that the error pointed out by the Panel that it had reimbursed the speaker the cost of two cokes and two teas despite the receipt indicating that on the balance of probabilities more than one person dined, was a regrettable oversight. This oversight resulted in the breach of Clauses 22.1 and 9.1, which Daiichi-Sankyo wholeheartedly apologised for. Daiichi-Sankyo should have maintained a higher standard but had failed to do. Daiichi-Sankyo would take all possible steps to avoid similar breaches of the Code in the future.

Daiichi-Sankyo submitted that the Panel had awarded the maximum possible ruling of a breach of Clause 9.1. The circumstances of this case did not warrant a breach of Clause 2. Breaches of Clause 2 related to matters judged to have brought discredit to, and reduction of confidence in, the industry. The Clause 2 supplementary information stated the following:

> 'A ruling of a breach of this clause is a sign of particular censure and is reserved for such circumstances. Examples of activities that are likely to be in breach of Clause 2 include prejudicing patient safety and/or public health, excessive hospitality, inducements to prescribe, unacceptable payments, inadequate action leading to a breach of undertaking, promotion prior to the grant of a marketing authorization, conduct of company employees/agents that fall short of competent care and multiple/cumulative breaches of a similar and serious nature in the same therapeutic area within a short period of time.'

Daiichi-Sankyo submitted therefore that its regrettable oversight did not come under the category of, or warranted, a breach of Clause 2 which was a sign of particular censure. With this in mind, Daiichi-Sankyo urged the Appeal Board to uphold the Panel's ruling of no breach of Clause 2 regarding this matter.

**FINAL COMMENTS FROM THE COMPLAINANT**

The complainant was somewhat disappointed by Daiichi-Sankyo's response which stated that it was not addressing the provision of the minivan for the family of the speaker because the complainant had not appealed Clause 23.1. However, the complainant noted previously that he/she did not understand why this would be considered under Clause 23.1 – instead it seemed to be an issue of hospitality and should, therefore, be considered under Clause 22.1.

The complainant noted that Daiichi-Sankyo also stated that it would not address the accommodation

issue because the complainant had not raised it in his/her initial complaint. The complainant stated that he/she knew nothing about the hotel or indeed the minivan until after he/she had complained, so these issues could not have been raised then. Now that the complainant had seen the responses from Daiichi-Sankyo, he/she should be able to ask more questions as part of the complaint.

The complainant alleged that Daiichi-Sankyo was using technicalities to avoid answering very legitimate questions about how it provided hospitality to family members of the speaker. The complainant enquired whether it was reasonable to think that the double room was only used for the speaker and not by his/her partner and why was the minivan provided for the whole family by Daiichi-Sankyo in the first place?

The complainant alleged that this went to the very heart of why big pharma got a bad name, as Daiichi-Sankyo had clearly been caught providing hospitality to the family members of the doctor, and now they were being obstructive in answering more questions about it. This most certainly reduced confidence in the industry which was why the complainant had appealed Clause 2.

The issue of confidentiality of the contract between Daiichi-Sankyo and the speaker was resolved by Daiichi-Sankyo agreeing that the PMCPA could provide the complainant with a redacted copy. The complainant was invited to make further comments on his/her appeal in relation to the redacted contract.

**APPEAL FROM THE COMPLAINANT – REDACTED CONTRACT**

The complainant noted that the contract had been heavily redacted and he/she was not even sure why Daiichi-Sankyo had bothered to provide this as it had cut out so much, it was meaningless. The complainant stated that Daiichi-Sankyo would want to take out the speaker's personal details, of course, but this level of redaction was absurd. Ironically even the section on transparency had been cut out.

The complainant noted that the only paragraph kept in stated that the speaker would be paid fees and expenses only to the extent agreed by the agreement. Elsewhere Daiichi-Sankyo had ticked transfers and catering/meals (organised by DSE only). The complainant assumed DSE stood for Daiichi-Sankyo Europe. The complainant alleged that Daiichi-Sankyo had admitted that it had provided transfers for the whole family, not just for the speaker. Daiichi-Sankyo had also submitted numerous receipts showing meals for more than one person which were clearly not organised by DSE. The complainant stated that it was obvious the speaker went with his/her family on these meals. Daiichi-Sankyo also ticked accommodation; the complainant questioned whether he/she could be sure that none of the family members used the speaker's room which the receipt stated was a double.

The complainant alleged that it appeared from the little of the contract Daiichi-Sankyo had chosen to reveal it had provided the speaker (and his/her family) more than agreed and he/she questioned what else was hidden in the redacted parts of the contract?

The complainant stated that he/she had never actually asked to see the contract in the first place, but now wondered what exactly Daiichi-Sankyo was trying to hide with so many redactions. This coupled with the obstructive nature of Daiichi-Sankyo's response to the appeal raised a lot of questions about this company and big pharma in general.

**COMMENTS FROM DAIICHI-SANKYO – REDACTED CONTRACT**

There were no further comments from Daiichi-Sankyo.

**APPEAL BOARD RULING**

The Appeal Board noted the importance of ensuring arrangements for fee for service activities for health professionals were carefully checked and that companies should have robust procedures in place in that regard. There was no prohibition in the Code regarding companies reimbursing health professionals when they made their own arrangements. Some companies did not permit this under their own policies and procedures. Similarly, some companies' policies prohibited accompanying persons when paying health professionals etc for fees for services. Whatever the individual arrangements companies needed to be confident that there was no breach of the Code. Contracts should clearly set out arrangements including what a company was prepared to pay for.

The Appeal Board noted that due to an error Daiichi-Sankyo had reimbursed the speaker for a proportion of the hospitality for his/her family and a breach of Clause 22.1 was ruled by the Panel which had also ruled a breach of Clause 9.1 in that high standards had not been maintained. The Appeal Board noted that Daiichi-Sankyo had allowed the speaker to make arrangements and pay for expenses to be later reimbursed. The Appeal Board considered that Daiichi-Sankyo should have carried out more robust checks and verification of the arrangements. The Appeal Board noted that external perception was important particularly if family members travelled with a health professional including when that health professional was fulfilling a fee for service commitment for a pharmaceutical company. However, despite these concerns the Appeal Board did not consider that the circumstances of this case were such as to warrant a breach of Clause 2 which was a sign of particular censure and it upheld the Panel's ruling of no breach of Clause 2. The appeal on this point was unsuccessful.

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| **Complaint received** | **17 July 2018** |
| **Case completed** | **22 May 2019** |

**CASE AUTH/3064/9/18**

# GILEAD SCIENCES v ViiV HEALTHCARE

## Promotion of Juluca

**Gilead Sciences Europe complained about the promotion of Juluca (dolutegravir/rilpivirine) by ViiV Healthcare. Juluca was a combination of two antiretroviral (ARV) medicines used in the treatment of human immune deficiency virus type-1 (HIV-1) infection in adults who were virologically-suppressed on a stable ARV regimen for at least 6 months. Gilead also marketed ARV combination medicines for the treatment of HIV.**

**The detailed response from ViiV is given below.**

**1 Reduction of antiretroviral (ARV) exposure and potential associated toxicities**

**Gilead complained about four similar statements within four different materials. Gilead stated that whilst each statement was slightly different, the following two claims were made in the context of the promotion of Juluca:**

**(i) reducing the number of ARV medicines from [not stated] to two would reduce a patient's ARV exposure;**

**(ii) this reduction translated into a reduction in potential associated toxicities.**

**Gilead alleged that these statements and claims were inaccurate, ambiguous, misleading, could not be substantiated and did not reflect the available evidence on adverse events.**

**The Panel considered each statement separately in the context of the material in which it appeared. The two allegations were ruled upon separately in each of the statements at issue.**

**A 'Streamline treatment with a 2-drug regimen & reduce your patients' ARV exposure & potential associated toxicities' (Juluca leavepiece (ref UK/DTGRPV/0006/18))**

**The Panel noted that the statement at issue included 'streamline' and further noted that ViiV had agreed following inter-company dialogue to withdraw materials that used this term. The Panel therefore made no ruling with regard to the reference to 'streamline'.**

**The Panel noted that the claim at issue appeared as a heading on the back page of a 4 page bi-folded A5 leavepiece which appeared to the Panel to be the final page that a user would read.**

**The Panel understood that drug exposure was a defined term in clinical pharmacology and it could be affected by numerous factors. The Panel noted that the statement at issue was in relation to ARV exposure and therefore encompassed all medicines within an ARV regimen. In the Panel's view, a reduction from a 3-medicine to a 2-medicine regimen reduced the number of ARV medicines that a patient was exposed to but it might not necessarily reduce the patient's ARV exposure as a measure of the concentration of ARV medicine in the body with respect to time; there were many factors to be considered, *inter alia*, dosage and interactions which could affect the clearance of one or more of the medicines in the regimen. Context and the audience were also important. The Panel noted that the statement at issue was below the caveat 'Based on the SWORD study results …'. The Panel further noted ViiV's submission that the SWORD studies included multiple ARV combinations in the comparator arm. The Panel noted, however, that the Llibre *et al* publication did not discuss exposure in subjects switching from triple therapy to dolutegravir/rilpivirine in terms of quantitative measures of total systemic drug exposure such as area under the curve (AUC). The Panel considered that the claim in question 'Streamline treatment with a 2-drug regimen & reduce your patients' ARV exposure and potential associated toxicities' was such that some HIV physicians might consider that there was pharmacokinetic drug exposure data for dolutegravir/rilpivirine versus the different triple therapy combinations in, *inter alia*, the SWORD studies and that was not so.**

**The Panel noted its comments above. In the Panel's view, and on balance, treatment with a two-medicine regimen did not necessarily mean that there was a reduction in ARV exposure versus treatment with a three-medicine regimen. The properties of each medicine in the regimen were relevant to ARV exposure. In this regard, the Panel considered that the reference to a two-drug regimen reducing ARV exposure versus a three-drug regimen in the claim 'Streamline treatment with a 2-drug regimen & reduce your patients' ARV exposure & potential associated toxicities' was ambiguous, unsubstantiated and a misleading comparison. Breaches of the Code were ruled.**

**The Panel noted Gilead's allegation regarding the claim in the second half of the statement at issue which suggested that a reduction in ARV exposure reduced potential associated toxicities.**

**The Panel noted that the Llibre *et al* publication referred to adverse events, including a breakdown from grade 1 to 4. The Panel considered that the use of the term 'toxicity' was ambiguous in relation to the SWORD study results and it was unclear if it related to a particular grade or type of adverse event.**

**The Panel noted that the preceding page of the**

leavepiece included the heading 'Juluca – reduce your patients' ARV exposure & potential associated toxicities' beneath which were claims regarding statistically significant recovery in bone mineral density and maintained lipid levels at 48 weeks. Within the same section of the leavepiece were statements related to adverse events, including rates of all adverse events, drug-related adverse events resulting in discontinuation and adverse events reported in >5% of subjects in the Juluca arm including psychiatric disorders, nasopharyngitis, headache and diarrhoea. The heading 'Juluca – reduce your patients' ARV exposure & potential associated toxicities', was separately subject to complaint at section B below; however, the Panel considered that this section of the leavepiece was relevant to the claim at issue on the back page (page 4). The Panel considered that the information on page 3 implied that the term 'toxicities' related to all types of adverse events and this implication was relevant to consideration of the claim in question on page 4.

The Panel noted that after switching to dolutegravir/rilpivirine, more subjects (77%) reported at least one adverse event by week 48 compared with subjects who continued with current ARVs (71%). Furthermore, adverse events stratified by grades 1 to 4 were either the same between the two treatment arms or higher with dolutegravir/rilpivirine.

The Panel noted that the statement at issue was below the caveat 'Based on the SWORD study results …' and in the Panel's view the claim 'Streamline treatment with a 2-drug regimen & reduce your patients' ARV exposure and potential associated toxicities' with regard to reduction in potential associated toxicities could not be substantiated by the SWORD study results.

The Panel noted its comments above. In the Panel's view, the implication that a two-medicine regimen reduced potential associated toxicities versus a three-medicine regimen in the claim 'Streamline treatment with a 2-drug regimen & reduce your patients' ARV exposure & potential associated toxicities' was ambiguous, unsubstantiated, did not reflect the available information about adverse events and was a misleading comparison. Breaches of the Code were ruled.

B 'Juluca-reduce your patients' ARV exposure and potential associated toxicities' (Juluca leavepiece (ref UK/DTGRPV/0006/18) and ViiV exchange website (ref UK/DTGRPV/0034/18(1))

Juluca leavepiece (ref UK/DTGRPV/0006/18)

The Panel considered that its comments and rulings above at Point A with regard to reduced ARV exposure applied here. In relation to the claim 'Juluca-reduce your patients' ARV exposure & potential associated toxicities', the Panel ruled breaches of the Code.

The Panel noted that in relation to reduced potential associated toxicities there were differences between the information presented on page 4 of the leavepiece and page 3 which included the claim at issue. The Panel noted its description of page 3 at Point A above. Pages 2 and 3 presented data from the SWORD 1 and 2 studies. The Panel considered that its comments above at Point A about reduced potential associated toxicities were relevant.

The Panel noted ViiV's submission that it refuted the allegation that the claim in question was too broad or all-encompassing as it specifically highlighted that the potential associated toxicities referred to were bone and lipid changes. The Panel noted its comments above, and at Point A. In the Panel's view, it was not clear in the leavepiece that 'toxicities' referred to only bone and lipid changes given that the same section of the leavepiece featured information on other adverse events including, *inter alia*, psychiatric disorders and diarrhoea. Furthermore, the Panel disagreed with ViiV's submission that the neutral effect on serum lipids in the dolutegravir/rilpivirine group could be considered as reduction in toxicity.

Noting its comments above, including at Point A, in the Panel's view, the implication that a two-medicine regimen reduced potential associated toxicities versus a three-medicine regimen in the claim 'Juluca- reduce your patients' ARV exposure & potential associated toxicities' was ambiguous, unsubstantiated, did not reflect the available information about adverse events, and was a misleading comparison. Breaches of the Code were ruled.

ViiV exchange website

The Panel noted that it was difficult from the materials provided to ascertain the different ways a user might navigate the website and therefore the order in which information would likely be read. The Panel noted that the statement 'Juluca-reduce your patients' ARV exposure & potential associated toxicities' appeared on a page which solely discussed bone health.

In relation to the claim 'Juluca-reduce your patients' ARV exposure …', the Panel noted its comments and rulings above at Point A which it considered applied here and ruled breaches of the Code.

In relation to the reduction in potential associated toxicities, the Panel considered that its comments at Point A above and its comments above (Point B in relation to the similar claim in the leavepiece) were relevant. The Panel noted that the only information on the webpage in question was in relation to bone health and focussed on the DEXA sub-study. In the Panel's view, the use of the plural to toxicity in the claim in question might imply that the term was used in relation to other toxicities in addition to bone. Furthermore, the Panel noted that the Juluca SPC stated in relation to this sub-study that any beneficial effect on fracture rate was not studied.

The Panel considered that the word 'associated' implied that the claimed potential reduction in toxicities was as a direct result of the claimed reduced ARV exposure. However, the data presented

**on the page in relation to effects on bone compared Juluca to those continuing on a TDF based regimen. The Panel noted Gilead's submission that there was evidence that switching from a TDF-based therapy to a different triple-based therapy was also associated with significant improvements in bone markers. In the Panel's view, the page implied that a reduction in ARV exposure in general would result in a reduction in potential associated toxicities, such as the effects on bone, however, it appeared to the Panel that the nature of the medicines was an important factor. Noting its comments above, in the Panel's view, the claim 'Juluca-reduce your patients' ARV exposure and potential associated toxicities' with regard to reduced potential associated toxicities was ambiguous, unsubstantiated, did not reflect the available information about adverse events and was a misleading comparison of Juluca with triple therapy. Breaches of the Code were ruled.**

**C '… streamline treatment and reduce ARV exposure for your virologically supressed HIV patients' (Journal detachable sleeve (ref VIIV/DTGRPV/0002/17b(1)c))**

**The Panel noted that the journal detachable sleeve featured a picture of a large rucksack next to a bench and a man walking away from the bench holding a smaller rucksack. In large font was the statement 'Progress with less' and below this it stated, in smaller font, 'Look inside and discover how to streamline treatment and reduce ARV exposure for your virologically suppressed HIV patients'.**

**The Panel noted that the sleeve had limited information. The reference to reduction in ARV exposure was not set within any context. There was no reference to moving from a three-medicine regimen to a two-medicine regimen. The Panel noted that the claim at issue included 'streamline' and noted its comments on this point above at Point A. Notwithstanding these comments, the Panel considered that the use of 'streamline' in the statement implied that there was a comparison being made with another type of treatment, although that treatment was not identified.**

**The Panel noted that the sleeve was associated with the advertisement published within the journal. However, the sleeve was a separate piece of material that needed to meet the requirements of the Code. The Panel noted its comments above at Point A and considered that the claim in question regarding '… reduce ARV exposure ...' was ambiguous, unsubstantiated and a misleading comparison of Juluca with other HIV treatments. Breaches of the Code were ruled.**

**D 'A 2-drug regimen may reduce ARV exposure and potential associated toxicities' (Juluca Fast Facts – ViiV exchange website (ref UK/DTGRPV/0005/18)).**

**The Panel noted the difference to the other statements considered above at points A, B and C in relation to ARV exposure; it stated 'may' reduce ARV exposure. The Panel noted its comments at points A and B above and considered that the use of the word 'may' did not make the claim any less ambiguous and ruled breaches of the Code.**
**In relation to the claim in question regarding reduction in potential associated toxicities, the Panel considered that it was not clear in the material what the term 'toxicities' related to. Whilst there was information on bone mineral density and lipid levels below the claim at issue, there was also information about adverse events including psychiatric disorders, nasopharyngitis, headache and diarrhoea to the left of it. In the Panel's view, in the context of this material, the term toxicities could imply any adverse event. The Panel noted its comments at Point B above in relation to lipids; in its view the neutral effect on serum lipids in the dolutegravir/rilpivirine group could not necessarily be considered a reduction in toxicity. The Panel further noted it comments at Point B above regarding the ViiV exchange website and the word 'associated'; it implied that the claimed potential reduction in toxicities was as a direct result of the claimed reduced ARV exposure. However, as previously noted above, it appeared to the Panel that the nature of the medicines in the regimen was a fundamental factor in relation to the effects on, *inter alia*, bone.**

**The Panel noted its comments at Point A above in relation to adverse events in the SWORD studies. In the Panel's view, the claim regarding reduction in potential associated toxicities could not be substantiated by the SWORD studies.**

**In the Panel's view, the implication in the claim 'a 2-drug regimen may reduce ARV exposure and potential associated toxicities' that a two-medicine regimen might reduce potential associated toxicities versus a three-medicine regimen was ambiguous, unsubstantiated, did not reflect the available information about adverse events and was a misleading comparison. Breaches of the Code were ruled.**

**2 Progress with less**

**Gilead complained about the following statements: 'For your virologically suppressed patients, PROGRESS WITH LESS (Juluca leavepiece (ref UK/DTGRPV/0006/18)) and 'PROGRESS WITH LESS' (Juluca advertisement (ref VIIV/DTGRPV/0002/17(1)a)).**

**Gilead submitted that in the claims at issue 'less' was not defined, was a hanging comparison and the claim, on its own and in the context in which it was used, implied that switching to Juluca was 'progressive', or an 'upgrade' and that a 2- medicine combination represented progress over a standard triple therapy ARV regimen. This impression was misleading, ambiguous and not capable of substantiation. Further, it created an unbalanced view that there were no risks attached to taking 'less'.**

**A For your virologically suppressed patients, PROGRESS WITH LESS (Juluca leavepiece (ref UK/DTGRPV/0006/18))**

**The Panel noted that the statement appeared on the front page of the A5 bi-folded leavepiece. 'Progress with less' was in large capital letters near the top of the leavepiece and directly above it, in smaller less prominent font, was the statement, 'For your virologically suppressed HIV patients'. Below the statement was a picture of a large rucksack next to a bench and a man walking away from the bench holding a smaller rucksack. Below the picture was the statement 'A new era of HIV treatment starts today'.**

**The Panel noted that Juluca was indicated in adults who had been virologically suppressed on a stable regimen for at least 6 months. The Panel noted that the licensed indication was difficult to read; however, the Panel considered that the claim at issue made it clear that Juluca was not for initial therapy.**

**The Panel noted Gilead's submission that 'less' was a hanging comparison. The Panel noted that although the page made it clear that Juluca was a two-medicine regimen, it was not made clear what Juluca was 'less' than. Only when the leavepiece was opened would the reader see information regarding the SWORD studies and that Juluca was compared to 3-drug regimens. In the Panel's view, the reader should not have to turn a page to see the qualification to a claim. This was particularly so when considering the main claim on the front page of a leavepiece.**

**The statement 'A new era of HIV treatment starts today', which featured below the picture, implied that there was a comparison being made between Juluca and another HIV treatment. In the Panel's view, it was not clear exactly which HIV treatment Juluca was been compared to in the claim 'Progress with less'. Furthermore, the term 'progress' when read in conjunction with the phrase 'new era' could imply some level of improvement versus the comparator, which was not supported by the SWORD studies which showed non-inferiority of Juluca compared to continued triple therapy.**

**Noting its comment above, in the Panel's view the claim 'For your virologically suppressed patients, PROGRESS WITH LESS' was ambiguous, a misleading comparison of Juluca with other HIV treatment and was not capable of substantiation, as alleged, and breaches of the Code were ruled.**

**The Panel noted Gilead's allegation that the claim created an unbalanced view that there were no risks attached to taking 'less'. The Panel noted that it was unclear what risks Gilead was referring to. The Panel noted ViiV's submission that there was no implication that there were no side-effects or risks to using Juluca and that the leavepiece made it clear that efficacy was no better than traditional triple therapy, all of which had a well-recognized risk of failure. The Panel considered that Gilead had not proved, on the balance of probabilities, that the claim in question created an unbalanced view that there were no risks to taking 'less' and ruled no breach of the Code.**

**B 'PROGRESS WITH LESS' (Juluca advertisement (ref VIIV/DTGRPV/0002/17(1)a))**

**The Panel noted that the journal advertisement had the same picture as described above at Point 2A. 'Progress with less' was in large capital letters near the top of the advertisement. Directly above it, in smaller less prominent font, was the statement, 'For your virologically suppressed HIV patients'. Below 'Progress with less' were two bullet points which stated, 'The first single-pill, 2-drug regimen powered by dolutegravir at the core' and 'Treatment non-inferior to traditional 3-drug regimens at maintaining virological suppression at 48 weeks.'**

**The Panel noted that, unlike the claim at Point 2A above, the bullet points qualified that 'less' was in relation to a 2 medicine-regimen versus a 3 medicine-regimen.**

**Whilst the Panel noted the differences between the advertisement in question and the claim in the leavepiece at Point 2A, the Panel still considered that the word 'progress' was ambiguous and misleading. The word could imply advancement of some sort and, in the Panel's view, the claim was a misleading and an unsubstantiated comparison of Juluca compared with triple therapy. Breaches of the Code were ruled.**

**The Panel considered that Gilead had not proved, on the balance of probabilities, that the claim 'PROGRESS WITH LESS' created an unbalanced view that there were no risks to taking 'less' as alleged and no breach of the Code was ruled.**

**3 2 well-tolerated agents**

**Gilead complained about the following claims: 'is now available with just 2 well tolerated agents' (Juluca leavepiece (ref UK/DTGRPV/0006/18)) and '2 well-tolerated agents, in 1 pill' (Juluca Fast Facts – ViiV exchange website (ref UK/DTGRPV/0005/18)).**

**Gilead alleged that the claims were misleading as they placed undue emphasis on the safety profile of the individual components of the Juluca two medicine regimen without clarifying the safety profile of the medicine being promoted.**

**A 'is now available with just 2 well tolerated agents' (Juluca leavepiece (ref UK/DTGRPV/0006/18))**

**The Panel noted that the claim at issue appeared on the back page, which appeared to be the final page of the bi-folded A5 leavepiece and was referenced to the dolutegravir and rilpivirine individual SPCs and not the Juluca SPC, however, the Juluca SPC was also included in the list of references.**

**The Panel noted that ViiV's submission quoted the European Public Assessment report and stated 'Based on all safety data submitted it is reasonable to conclude that the safety profile of the combined administration of DTG [dolutegravir] and RPV [rilpivirine] seems to be consistent with the established safety profiles and the current labelling of the single agents. No additional risks or safety issues were identified'.**

**The Panel noted ViiV's submission that the SWORD studies were conducted using the separate licensed**

**agents, dolutegravir and rilpivirine, as opposed to the fixed dose combination and that the Juluca European Medicines Agency (EMA) licence was underpinned by the SWORD 1 and 2 studies.**

**The Panel noted that page 3 of the leavepiece detailed safety results from the SWORD studies including the rates of adverse events, drug-related adverse-events resulting in discontinuation (Juluca 4% vs continued 3-drug regimens <1%), and adverse events reported in ≥ 5% of subjects in the Juluca arm (psychiatric disorders 12%, nasopharyngitis 10%, headache 8% and diarrhoea 6%). Page 3 of the leavepiece also stated that in studies supporting Juluca, dolutegravir 50mg and rilpivirine 25mg were used and that bioequivalence with Juluca had been demonstrated. The Panel noted that, nonetheless, the claim should be capable of standing alone.**

**The Panel noted its comments above and did not consider that the claim at issue 'is now available with just 2 well tolerated agents', in the context of the leavepiece, was misleading by virtue of the emphasis on the individual components without clarifying the safety profile of Juluca, as alleged. No breach of the Code was ruled.**

**B '2 well-tolerated agents, in 1 pill' (Juluca Fast Facts – ViiV exchange website (ref UK/DTGRPV/0005/18))**

**The Fast Facts sheet referred to the SWORD studies including: design, the rates of adverse events in the two treatment arms, rates of drug-related adverse events resulting in discontinuation, adverse events reported in ≥5% of subjects in the Juluca arm and that bioequivalence of Juluca to dolutegravir 50mg and rilpivirine 25mg had been demonstrated.**

**The Panel noted its comments above at Point 3A. The Panel did not consider that the claim '2 well-tolerated agents, in 1 pill' in the context of the material was misleading by virtue of the emphasis on the individual components without clarifying the safety profile of Juluca, as alleged. No breach of the Code was ruled.**

**4 Size of tablet claim**

**Gilead complained about the claim 'All in 1 small pill' (Juluca leavepiece (ref UK/DTGRPV/0006/18)).**

**Gilead submitted that the claim was ambiguous as it did not clarify the actual dimensions of the Juluca tablet. Without this clarification Gilead also considered the claim was a hanging comparison, as it was unclear to the reader in comparison to what the tablet was considered small.**

**The Panel noted that the claim at issue featured on the back page of the bi-folded A5 leavepiece. The Panel noted that the dimensions of Juluca, as stated in the SPC, were 14 x 7mm. The Panel noted ViiV's submission that Juluca was the smallest complete single-pill HIV regimen. The Panel further noted that ViiV referred to a study by Jacobson *et al* (2016) on the sizes of commonly prescribed paediatric medicines; ViiV submitted that Juluca was comparably on the smaller spectrum of medicines available for children. The Panel noted that Jacobson *et al* stated that common paediatric antibiotics ranged from 8 to 25mm in length, median 17mm. The Panel further noted that Juluca was indicated for use in adults only.**

**In the Panel's view, the description 'small' was somewhat subjective, however, the Panel did not consider that the claim was ambiguous by not stating the dimensions, as alleged. The audience was an important consideration. Noting its comments above, the Panel did not consider that the claim 'All in one small pill' was a hanging comparison or that Gilead had proved, on the balance of probabilities, that the description would be misleading to the intended audience, HIV physicians. No breach of the Code was ruled.**

**5 High standards**

**Gilead submitted that, generally, in relation to all of the above issues, ViiV had failed to maintain high standards.**

**The Panel noted its comments and rulings of breaches of the Code at Points 1 and 2 above. In the Panel's view, ViiV had failed to maintain high standards and a breach of the Code was ruled.**

Gilead Sciences Europe Limited complained about the promotion of Juluca (dolutegravir/rilpivirine) by ViiV Healthcare. Juluca was a combination of two antiretroviral (ARV) medicines used in the treatment of human immune deficiency virus type-1 (HIV-1) infection in adults who were virologically-suppressed on a stable ARV regimen for at least 6 months. Gilead also marketed ARV combination medicines for the treatment of HIV.

Gilead stated that inter-company dialogue with ViiV had been unsuccessful on a number of matters which it was now raising as a complaint.

**1 Reduction of antiretroviral (ARV) exposure and potential associated toxicities**

Gilead complained about the following statements: 'Streamline treatment with a 2-drug regimen & reduce your patients' ARV exposure & potential associated toxicities' (Juluca leavepiece (ref UK/DTGRPV/0006/18)); 'Juluca – reduce your patients' ARV exposure & potential associated toxicities' (ViiV exchange website (ref UK/DTGRPV/0034/18(1))); '… streamline treatment and reduce ARV exposure for your virologically supressed HIV patients' (Journal detachable sleeve (ref VIIV/DTGRPV/0002/17b(1)c)); 'A 2- drug regimen may reduce ARV exposure and potential associated toxicities' (Juluca Fast Facts – ViiV exchange website (ref UK/DTGRPV/0005/18)).

**COMPLAINT**

Gilead stated that whilst each statement was slightly different, the following two claims were made in the context of the promotion of Juluca, a combination of two medicines for the treatment of HIV in virally suppressed patients:

(iii) reducing the number of ARV medicines from [not stated] to two would reduce a patient's ARV exposure;
(iv) this reduction translated into a reduction in potential associated toxicities.

Gilead considered these statements and claims were inaccurate, ambiguous, misleading, could not be substantiated and did not reflect the available evidence on adverse events, in breach of Clauses 7.2, 7.3, 7.4 and 7.9 of the Code.

Gilead submitted that the claim that moving to a two-medicine regimen would reduce a patient's ARV exposure was stated without any qualification and as such asserted that this would always be the case, regardless of which medicines the patient switched from and which medicines the patient switched to. Whilst a switch to a two-medicine regimen reduced the number of ARV medicines being taken by the patient, Gilead did not accept that this would necessarily reduce the patient's ARV exposure and such a claim must be substantiated.

The extent of ARV exposure was not measured by the number of individual medicines being taken but by the amount of ARV the patient was exposed to by the regimen he/she took. Factors such as the amount of active ingredient in each ARV medicine were also relevant to the level of ARV exposure.

Further, when considering ARV exposure, both the pharmacokinetic and pharmacodynamic properties of the medicines must be considered (ie both medicine plasma/tissue levels and the pharmacodynamic properties of the individual components). This was particularly relevant in the context of any comparison between three medicine regimens and two medicine regimens when the components of each of the regimens did not match (and even if they did, there should be no interaction that affected the pharmacokinetic properties of each of the remaining components when switching from 3 to 2 medicines). In other words, ARV exposure could only be discussed as a potential variable if there was a comparison between a 3 medicine and 2 medicine combination comprising of the same components, and where the pharmacokinetics of each of the remaining components were unaffected by the removal of a third medicine.

The main clinical study data for Juluca was the SWORD study (Llibre *et al* 2018). No data on the pharmacokinetic assessment on the individual components had been presented in the context of that study or supplied in response to this complaint. Instead, the SWORD study involved a switch from a triple combination HIV regimen (ie three medicines) to a regimen of dolutegravir and rilpivirine; 87% of patients who switched to dolutegravir and rilpivirine had not previously been exposed to those two medicines and so switched to two medicines that had different pharmacokinetic and pharmacodynamic properties compared with their original triple regimens.

Gilead stated that the claim that switching to a two-medicine regimen would reduce potential associated toxicities was also stated without any qualification and claimed, both generally and specifically in relation to Juluca, that a switch to a two medicine ARV regimen would result in a reduction of potential toxicities.

For the reasons identified above, Gilead did not accept that a switch from triple therapy to two ARV medicines would necessarily reduce a patient's ARV exposure. Further, as the two medicines combined in Juluca (dolutegravir and rilpivirine) might have different pharmacokinetic and pharmacodynamic properties to the original three ARV medicines the patient was switched from, Gilead considered it was misleading to assert that any differences in tolerability or safety that might arise from the switch to two medicines were a general function of reduced ARV exposure. This was an inaccurate, misleading and ambiguous claim.

In any event, the claim that a switch to Juluca would reduce potential associated toxicities must be substantiated. The SWORD study demonstrated that numerically more participants who switched to dolutegravir and rilpivirine reported adverse events leading to withdrawal when compared with patients remaining on triple regimens (17 (3%) vs 3 (<1%)). As a further example, in the SWORD study, neuropsychiatric adverse events were observed to be significantly increased in patients who switched to Juluca - 61 (12%) psychiatric disorders vs 32 (6%) in the control arm; further, 7 discontinuations for psychiatric disorders and 1 discontinuation for nervous system disorders occurred in the Juluca arm vs 1 discontinuation due to psychiatric disorders in the control arm at 48 weeks.

The prominent focus on the 'potential' benefit of 'reducing ARV exposure' on toxicity without balancing appropriately with the potential risks was misleading and unbalanced, and the use of the broad term 'toxicity' without clarification as to what level of adverse event was considered to fall within the term, made the claim ambiguous.

Clarification and qualification was required as there was no universally accepted definition of 'toxicity'. It was clear from studies relating to dolutegravir that the term was not reserved for events that resulted in permanent damage or long-term harm – eg the seminal Dutch study, 'Unexpectedly High Rate of Intolerance for Dolutegravir in Real Life Setting', (Van den Berk *et al* 2016), a poster presented at AIDS 2016 (de Boer *et al* 2016), and an associated peer reviewed publication on a German cohort study (Hoffmann *et al* 2017, 'Higher rates of neuropsychiatric adverse events leading to dolutegravir discontinuation in women and older patients') which described the real world clinical experience of dolutegravir – one of the components of Juluca – the authors characterised the gastrointestinal and/or neuropsychiatric side-effects observed with dolutegravir as 'toxicities' even though they emerged over a median of 78 days, or within 12 months, respectively.

Further, all claims made the generalisation that there was a potential for reduced toxicity when switching from any combination of three medicines to Juluca, without clarification that the ARV medicines being switched from and to was relevant, and the claims

failed to adequately disclose that the majority (70%) of patients on triple therapy in the SWORD study were on a tenofovir disoproxil fumarate (TDF)-based regimen. A large body of evidence supported that switching from TDF-based therapy (a therapy associated with renal events and bone loss) to emtricitabine/tenofovir alafenamide (F/TAF) based triple therapy was also associated with significant improvements in renal and bone markers, which further highlighted that the nature of medicines used was important in reducing potential toxicities, not just the number of medicines.

Whilst information about adverse events, bone mineral density and DEXA measures was included in the UK leavepiece (ref UK/DTGRPV/0006/18) immediately after the phrase 'reduce your patients' ARV exposure and potential associated toxicities', this was not always the case, eg the Juluca fast facts infographic from the ViiV Exchange website (UK/DTGRPV/0005/18) and even with the UK leavepiece, Gilead asserted that this did not provide adequate clarification and qualification for the broad claim of 'reduce potential associated toxicities' due to:

- the prominence of that claim on pages 3 and 4 of the piece
- unqualified use of 'toxicities' as distinct from 'safety' as outlined above
- the all-encompassing title which implied that a number of safety (toxicity) issues could be avoided, even though the only substantiating evidence was an improvement in bone mineral density and renal at week 48, restricted to those patients who were switched from a TDF-based triple ARV regimen. Gilead did not accept that maintenance of lipid levels could reasonably be claimed as avoiding future safety issues vs comparator
- an imbalance in the prominence of the rates of neuropsychiatric toxicity observed with Juluca on page 3
- the characterisation of the rates of neuropsychiatric toxicity observed with Juluca on page 3 ('few' medicine-related adverse events resulted in discontinuation).

The clear communication objective of all of the campaign pieces was to assert that by switching from ARV triple therapy to Juluca, there was always a reduction in ARV exposure which translated to a potential (or actual) reduction [sic?] in tolerability or safety. Any statements of this nature that made any relevant claims around potential improvements in long-term safety must be limited to those which were accurate, balanced, objective, unambiguous and capable of substantiation and Gilead did not consider this test had been met in the Juluca promotional material in question. Gilead alleged breaches of Clauses 7.2, 7.3, 7.4 and 7.9.

**RESPONSE**

ViiV submitted that Gilead seemed to have conflated a number of claims and pieces of material into one overarching complaint whilst acknowledging each statement was slightly different. Gilead had alleged breaches of the Code in relation to the claim that reducing the number of ARV medicines from three to two would reduce a patient's ARV exposure. ViiV stated that it strongly refuted this allegation for general and specific reasons.

ViiV refuted the allegations in general as it considered that the statement that changing from three ARVs to two ARVs would represent a reduction in exposure to ARVs was self-evident.

ViiV also considered that the concept was clearly understood by HIV physicians. In the scientific literature, commonly studied and cited approaches to reducing ARV exposure without compromising the efficacy of treatment included reducing the number of medicines within a regimen.

ViiV explained that over the past twenty years HIV physicians had prescribed a combination of three or even four ARVs to be taken together to suppress the HIV virus. Different AVRs had been used simultaneously to minimise the chance that the virus developed resistance to treatment. But, as the treatment of HIV was currently life-long, and all treatments carried risks as well as benefits, there was concern that this polypharmacy approach might lead to significant long-term toxicities for patients. Hence there was interest in various simplification strategies to reduce the patient's exposure to ARVs including reducing the number of medicines used.

ViiV noted that Gilead had tried to complicate this reality with a discussion of the ingredients, pharmacokinetic and pharmacodynamic properties of individual medicines. Yet regardless of the individual properties of an ARV – all currently available ARVs required daily dosing which suggested broadly similar exposure to them from a patient and clinical perspective – a reduction from three to two medicines still represented reduced exposure to whatever those cumulative properties might be.

ViiV noted that Gilead failed to provide any specific evidence where reducing the ARV number from three to two resulted in any outcome other than a decrease in ARV exposure.

More specifically ViiV disputed the allegations in relation to the use of the term 'reduced ARV exposure' in the promotion of Juluca. Firstly, Juluca was a two-medicine regimen of dolutegravir and rilpivirine. Secondly, the available data supported its use as an effective treatment in certain HIV-positive patients. The Juluca FDA/EMA licence was underpinned by the SWORD 1 and 2 studies; these two, fully powered, randomised controlled trials recruited patients with a suppressed viral load who had taken conventional HIV treatment containing at least three medicines and successfully switched them to the two-medicine regimen of dolutegravir and rilpivirine, thereby reducing exposure through reducing the number of medicines within their treatment regimen while maintaining viral suppression. There were also several peer reviewed publications which described the rationale for reducing exposure and referenced dolutegravir plus rilpivirine and the SWORD studies.

ViiV noted that on the Juluca leavepiece, the ViiV exchange website and on the ViiV exchange Juluca

Fast-Facts, the claims of reducing ARV exposure were made clearly within the context of switching therapy from the standard three ARVs to Juluca, a two-medicine regimen. The study design was included and multiple references were made with respect to switching from three to two medicines.

In the advertisement (ref VIIV/DTGRPV/0002/17(I) a), the claims of reducing ARV exposure were made clearly within the context of switching therapy from the standard three ARVs to Juluca, a two-medicine regimen with two prominent bullet points immediately beneath the headline indicating that Juluca was the first single pill, two medicine regimen and it had shown non-inferiority to traditional three medicine regimens. The materials were aimed at expert HIV physicians who well understand that current standard regimens contain three or four ARVs and therefore Juluca being a complete regimen consisting of only two ARVs was clearly less ARV exposure.

ViiV noted that Gilead had further alleged breaches of the Code in relation to the claim that a reduction in ARVs translated into a reduction in potential associated toxicities.

ViiV strongly refuted the allegation for general and specific reasons. ViiV's general reasoning was that logic dictated that reducing the number of ARVs from three or four to two resulted in decreased exposure to ARVs and the toxicities related to them.

ViiV stated that those involved in HIV care would reach the same conclusion. For example, ViiV noted that a UK HIV physician, currently President of the International AIDS Society, referred to the use of two rather than three ARVs in the August 2018 British Medical Journal article by simply stating *'You reduce toxicity'* (Pozniak, 2018).

Similarly, in the Lancet, Llibre *et al* (2018) made it clear that use of Juluca would avoid the major NRTI (nucleoside reverse transcriptase inhibitors) toxicities; 'Once-daily oral dolutegravir-rilpivirine would be the first oral two-drug regimen that provides patients with an alternative to guideline-preferred triple-drug regimens, avoids major NRTI toxicities, has limited potential for drug-drug interactions, and does not increase lipid concentrations or inflammatory biomarkers'.

ViiV noted that Gilead had referred to adverse events and toxicity interchangeably in its complaint. ViiV disagreed with this approach as it observed that adverse events and toxicity were often considered separately in both the reporting of HIV studies and in practice by HIV physicians. In fact, Gilead also made this distinction when it reported adverse events and toxicity in a number of publications.

More specifically Gilead suggested that the adverse event reports from the SWORD 1 and 2 studies did not support claims related to reduced toxicity of dolutegravir and rilpivirine. Gilead noted that numerically more participants switching to dolutegravir and rilpivirine reported adverse events leading to withdrawal when compared with patients remaining on triple therapy.

In response, and in addition to highlighting again the bundling of the terms adverse events and toxicity, ViiV stated that an explanation for these adverse event findings resided more in the study design than the characteristics of the medicines themselves. The Committee for Medicinal Products for Human Use (CHMP) at the European Medicines Agency recognised in the European Public Assessment Report (EPAR) for Juluca the particular difficulties of reporting adverse events in an open-label switch trial, where the comparator arm remained on therapy that the patients had been stable on for at least six months, stating 'Firstly, it can be assumed that many AEs occur at the beginning of therapy so that subjects on stable therapy (i.e. subjects in the CAR ["Current antiretroviral"] treatment group) would report less AEs than those randomised to a new therapy regimen (i.e. subjects in the dolutegravir and rilpivirine treatment group). Comparing subjects stable on CAR with subjects newly switched to dolutegravir and rilpivirine can therefore be expected to create a bias in favour of CAR. An analysis of the timing of occurrence of adverse events relative to the start of dolutegravir and rilpivirine / CAR treatment showed a shorter median time to onset in the dolutegravir and rilpivirine group compared to the CAR group. This observation reinforces the assumption that the higher incidence of AEs in the dolutegravir and rilpivirine treatment group vs CAR group is mainly due to the fact that subjects in the dolutegravir and rilpivirine group were not familiar with the adverse events of this treatment while the subjects on the CAR arm were already on their regimen for at least 6 months and thereby somewhat selected for tolerating the treatment'.

In terms of toxicities themselves the safety analyses of the SWORD 1 and 2 studies showed an improvement in a marker of toxicity as Gilead acknowledged in its complaint ('… the only substantiating evidence is an improvement in BMD and renal at week 48 …'). The studies focused on some of the established long-term toxicities associated with ARVs, ie bone destruction (primarily a toxicity of NRTIs) and altered lipids (primarily a toxicity of protease inhibitors). As stated in the Juluca summary of product characteristics (SPC), the mean bone mineral density (BMD) increased in a DEXA sub-study from baseline to week 48 in subjects who switched to dolutegravir and rilpivirine (1.34% total hip and 1.46% lumbar spine) compared with those who continued on treatment with a tenofovir disoproxil fumarate (TDF) containing antiretroviral regimen, and thus indicated a reduction in the well-established deleterious effect on BMD that NRTIs might have. With respect to the maintenance of lipid levels, this was relevant as TDF was well recognised to be beneficial in lowering lipid levels and ViiV considered that it was important to demonstrate that this benefit was maintained when switching to dolutegravir and rilpivirine. The authors stated: '… we noted a neutral effect on serum lipids in the dolutegravir- rilpivirine group, despite more than 70% of these participants being switched from tenofovir disoproxil fumarate, which has been

reported to be a lipid-friendly drug'.
ViiV noted that Gilead also commented that in the study population within SWORD 1 and 2, 70% of patients took a triple regimen which included TDF and that another combination of ARVs was also associated with significant improvements in renal and bone markers when compared to TDF-containing regimens. Gilead was referring to the use of tenofovir alafenamide (TAF), another pro-drug of tenofovir which was still an NRTI, a type of ARV which was well recognized as having the potential for deleterious long-term effects such as bone or renal toxicity. Juluca was the only licensed regimen that was NRTI-sparing and therefore although TAF might have less impact on these areas than TDF, it was still an NRTI and carried some risk of NRTI toxicities.

ViiV noted that the SWORD studies included multiple ARV combinations; the predominance of TDF was consistent with practice within the UK given it was the most commonly used NRTI in the UK and was a preferred agent in combination with other ARVs in both the British HIV Association and multiple international guidelines. This significant reversal in bone toxicity when switching away from a TDF containing regimen was a proxy for how avoidance of an additional medicine in any regimen could prevent known or unknown toxicities that might be attributed to that medicine.

ViiV noted Gilead's various allegations regarding the manner of presentation of the claims 'reduce potential associated toxicities' in the leavepiece [UK/DTGRPV/0006/18]. ViiV disagreed that the claim was too broad or all-encompassing as the company specifically highlighted that potential associated toxicities referred to bone and lipid changes.

Gilead also asserted there was an 'imbalance in the prominence of the rates of neuropsychiatric disorders in the leavepiece', but the commonest adverse events (those occurring in >5%) in the Juluca arm were clearly listed with similar prominence to other adverse events, along with the frequency of their occurrence. The first of these was psychiatric (12%), reflecting Table 2 of the publication of the SWORD 1 and 2 studies.

Gilead also had concerns over 'the characterisation of the rates of neuropsychiatric toxicity observed with Juluca on page 3 ("few"' drug-related AEs resulted in discontinuation)'. The characterisation of the rates was specific and clear – the bullet point clearly stated 'psychiatric disorders (12%)'. Of these, the authors stated 'Most neuropsychiatric adverse events were grade 1 or 2 and not considered to be related to dolutegravir/rilpivirine'.

ViiV submitted that the discontinuations due to medicine-related adverse events was clearly stated as being 3%, so readers were in no doubt what was meant by 'few'. Of these only 1% were due to psychiatric disorders.

In summary, ViiV believed that a change from three to two of the currently available ARVs could appropriately be described as reducing exposure to them and their associated potential toxicities, that it was appropriate to make such claims with Juluca, that the information was presented in fair and balanced manner and that ultimately there was no breach of Clauses 7.2, 7.3, 7.4 and 7.9.

**PANEL RULING**

The Panel noted Gilead's allegation that four similar statements were in breach of the Code. The Panel noted that there were two overarching allegations: the claim that reducing the number of ARV medicines in a regimen from three to two would reduce a patient's ARV exposure, and the claim that this reduction translated into a reduced potential for associated toxicities.

The Panel considered each statement separately in the context of the material in which it appeared.

The two allegations were ruled upon separately in each of the statements at issue.

**A 'Streamline treatment with a 2-drug regimen & reduce your patients' ARV exposure & potential associated toxicities' (Juluca leavepiece (ref UK/DTGRPV/0006/18))**

The Panel noted that the statement at issue included 'streamline' and further noted that ViiV had agreed following inter-company dialogue to withdraw materials that used this term. The Panel therefore made no ruling with regard to the reference to 'streamline'.

The Panel noted that the claim at issue appeared as a heading on the back page of the 4 page bi-folded A5 leavepiece which appeared to the Panel to be the final page that a user would read. Above the claim at issue, in smaller less prominent font, was the statement, 'Based on the SWORD study results …' and below the claim at issue were three further statements, in numerical descending bullet points: 'Juluca is non-inferior to 3-drug regimens at maintaining virological suppression …', is now available with just 2-well-tolerated agents …', 'all in 1 small pill'.

The Panel noted that SWORD-1 and SWORD-2 were Phase III, open-label, randomised, 48-week studies which demonstrated that dolutegravir 50mg plus rilpivirine 25mg (a two-drug regimen) was non-inferior to the continuation of triple ARV therapy (two nucleoside reverse transcriptase inhibitors plus either an integrase strand transfer inhibitor, non-nucleoside reverse transcriptase inhibitor or protease inhibitor) in maintaining virological suppression over 48 weeks, in adults who had been stable for at least 6 months (Llibre *et al*, 2018). The Panel noted ViiV's submission that the Juluca European Medicines Agency licence was underpinned by the SWORD-1 and SWORD-2 studies and that Juluca had demonstrated bioequivalence to dolutegravir 50mg plus rilpivirine 25mg.

The Panel noted Gilead's assertation that switching from a three-medicine regimen to a two-medicine regimen reduced the number of ARV medicines taken by a patient but did not necessarily reduce the patient's ARV exposure and such a claim required

substantiation. The Panel further noted Gilead's submission that the extent of ARV exposure was not measured by the number of individual medicines but by the amount of ARV the patient was exposed to by the regimen and factors such as amount of active ingredient in each ARV, and the pharmacokinetic and pharmacodynamic properties of the medicines was relevant to the level of ARV exposure. The Panel noted Gilead's assertation that ARV exposure could only be discussed as a potential variable if there was a comparison between a 3-medicine and a 2-medicine combination comprising of the same components, and where the pharmacokinetics of each of the remaining components was unaffected by the removal of the third medicine. Gilead had argued that no data on the pharmacokinetics of the individual components had been presented in the context of the SWORD studies or supplied by ViiV in response to the complaint. Furthermore, 87% of patients who switched to dolutegravir/rilpivirine from triple therapy had not previously been exposed to these two medicines, which had different pharmacokinetic and pharmacodynamic properties compared to the original 3 medicines the patient had taken.

The Panel noted ViiV's response that it was a self-evident statement of fact that changing from three to two ARVs represented a reduction in exposure to ARVs; all those currently available required daily dosing suggesting broadly similar exposure and a reduction from three to two medicines still represented reduced exposure to whatever those cumulative properties might be. ViiV noted that Gilead had not provided any specific evidence where a reduction from three to two ARVs resulted in any outcome other than a decrease in ARV exposure.

The Panel noted that neither ViiV nor Gilead had referred to any specific pharmacokinetic data. The Panel considered that ViiV had taken a very general view of the claim in question and had not addressed Gilead's point about the pharmacokinetics and pharmacodynamics of individual medicines in a regimen and overall ARV exposure.

The Panel noted that the published literature supplied by ViiV discussed different ways ARV exposure could be reduced, which included, *inter alia*, reference to fewer drugs (Katlama *et al* 2017) and the Panel noted ViiV's submission that this was a concept clearly understood by HIV physicians. It appeared to the Panel that the published literature provided by ViiV used terminology that suggested fewer medicines in an ARV regimen translated into reduced ARV exposure, without considering the specific properties of each medicine in the regimen. The Panel noted that, nonetheless, matters that appeared in published peer-reviewed journals might be found in breach of the Code when featured in company material.

The Panel understood that drug exposure was a defined term in clinical pharmacology and it could be affected by numerous factors. The Panel noted that the statement at issue was in relation to ARV exposure and therefore encompassed all medicines within an ARV regimen. In the Panel's view, a reduction from a 3-medicine to a 2-medicine regimen reduced the number of ARV medicines that a patient was exposed to but it might not necessarily reduce the patient's ARV exposure as a measure of the concentration of ARV medicine in the body with respect to time; there were many factors to be considered, *inter alia*, dosage and interactions which could affect the clearance of one or more of the medicines in the regimen. Context and the audience were also important. The Panel noted that the statement at issue was below the caveat 'Based on the SWORD study results …'. The Panel further noted ViiV's submission that the SWORD studies included multiple ARV combinations in the comparator arm. The Panel noted, however, that the Llibre *et al* publication did not discuss exposure in subjects switching from triple therapy to dolutegravir/rilpivirine in terms of quantitative measures of total systemic drug exposure such as area under the curve (AUC). The Panel considered that the claim in question 'Streamline treatment with a 2-drug regimen & reduce your patients' ARV exposure and potential associated toxicities' was such that some HIV physicians might consider that there was pharmacokinetic drug exposure data for dolutegravir/rilpivirine versus the different triple therapy combinations in, *inter alia*, the SWORD studies and that was not so.

The Panel noted its comments above. In the Panel's view, and on balance, treatment with a two-medicine regimen did not necessarily mean that there was a reduction in ARV exposure versus treatment with a three-medicine regimen. The properties of each medicine in the regimen were relevant to ARV exposure. In this regard, the Panel considered that the reference to a two-drug regimen reducing ARV exposure versus a three-drug regimen in the claim 'Streamline treatment with a 2-drug regimen & reduce your patients' ARV exposure & potential associated toxicities' was ambiguous, unsubstantiated and a misleading comparison. Breaches of Clauses 7.2, 7.3 and 7.4 were ruled.

The Panel noted Gilead's allegation regarding the claim in the second half of the statement at issue which suggested that a reduction in ARV exposure reduced potential associated toxicities.

The Panel noted Gilead's submission that there was no universally accepted definition of toxicity. The Panel noted Gilead's argument that the broad term 'toxicity' without any clarification as to what level of adverse event was considered to fall within the term made the claim ambiguous. Furthermore, the Panel noted Gilead's allegation that all claims made the generalisation that there was a potential for reduced toxicity when switching from any combination of three medicines to Juluca; and ViiV had failed to adequately disclose that the majority (70%) of patients on triple therapy in the SWORD studies were taking a tenofovir disoproxil fumarate (TDF) based regimen, which was associated with renal events and bone loss.

The Panel noted Gilead's argument that there was a large body of evidence that switching from a TDF-based therapy to a different triple-based therapy

(emtricitabine/tenofovir alafenamide) was also associated with significant improvements in renal and bone markers which highlighted that the nature of drugs, not just the number of drugs, was relevant in relation to reducing potential toxicities. The Panel noted ViiV's submission that Juluca was the only licensed regimen that was NRTI-sparing and that the significant reversal in bone toxicity when switching away from a TDF containing regimen was a proxy for how avoidance of an additional medicine in any regimen could prevent known or unknown toxicities that might be attributed to that medicine.

The Panel noted that the Llibre *et al* publication referred to adverse events, including a breakdown from grade 1 to 4. The Panel considered that the use of the term 'toxicity' was ambiguous in relation to the SWORD study results and it was unclear if it related to a particular grade or type of adverse event.

The Panel noted ViiV's submission that logic dictated that reducing the number of ARVs from four/three to two resulted in decreased exposure to ARVs and the toxicities related to them. In the Panel's view, the profile of the medicines moved from and to needed to be acknowledged and the use of the word 'potential' in reference to toxicities did not remove the need for substantiation. The Panel noted ViiV's submission that the SWORD studies showed improvements in long-term toxicities associated with ARVs, namely bone destruction, which was primarily a toxicity of NRTIs, and altered lipids, which was primarily a toxicity of protease inhibitors.

The Panel noted that the bottom half of page 3, the preceding page of the leavepiece, had the heading 'Juluca – reduce your patients' ARV exposure & potential associated toxicities' beneath which were claims regarding statistically significant recovery in bone mineral density and maintained lipid levels at 48 weeks. Within the same section of the leavepiece were statements related to adverse events, including rates of all adverse events, drug-related adverse events resulting in discontinuation and adverse events reported in >5% of subjects in the Juluca arm including psychiatric disorders, nasopharyngitis, headache and diarrhoea. The heading 'Juluca – reduce your patients' ARV exposure & potential associated toxicities', was separately subject to complaint at section B below; however, the Panel considered that this section of the leavepiece was relevant to the claim at issue on the back page (page 4). The Panel considered that the information on page 3 implied that the term 'toxicities' related to all types of adverse events and this implication was relevant to consideration of the claim in question on page 4.

The Panel noted that after switching to dolutegravir/rilpivirine, more subjects (77%) reported at least one adverse event by week 48 compared with subjects who continued with current ARVs (71%). Furthermore, adverse events stratified by grades 1 to 4 were either the same between the two treatment arms or higher with dolutegravir/rilpivirine. The Panel noted ViiV's submission that it could be assumed that many adverse events occur at the beginning of therapy so that subjects continuing on current ARV therapy would report less adverse events than those randomised to a new therapy (ie the dolutegravir/rilpivirine group). The Panel noted that the statement at issue was below the caveat 'Based on the SWORD study results …' and, in the Panel's view, the claim 'Streamline treatment with a 2-drug regimen & reduce your patients' ARV exposure and potential associated toxicities' with regard to reduction in potential associated toxicities could not be substantiated by the SWORD study results.

The Panel noted its comments above. In the Panel's view, the implication that a two-medicine regimen reduced potential associated toxicities versus a three-medicine regimen in the claim 'Streamline treatment with a 2-drug regimen & reduce your patients' ARV exposure & potential associated toxicities' was ambiguous, unsubstantiated, did not reflect the available information about adverse events and was a misleading comparison. Breaches of Clauses 7.2, 7.3, 7.4 and 7.9 were ruled.

**B 'Juluca-reduce your patients' ARV exposure and potential associated toxicities' (Juluca leavepiece (ref UK/DTGRPV/0006/18) and ViiV exchange website (ref UK/DTGRPV/0034/18(1))**

**Juluca leavepiece (ref UK/DTGRPV/0006/18)**

The Panel considered that its comments and rulings above at Point A with regard to reduced ARV exposure applied here. In relation to the claim 'Juluca-reduce your patients' ARV exposure & potential associated toxicities', the Panel ruled a breach of Clauses 7.2, 7.3 and 7.4.

The Panel noted that in relation to reduced potential associated toxicities, there were differences between the information presented on page 4 of the leavepiece and page 3 which included the claim at issue. The Panel noted its description of page 3 at Point A above. Pages 2 and 3 presented data from the SWORD 1 and 2 studies. The Panel considered that its comments above at Point A about reduced potential associated toxicities were relevant.

The Panel noted Gilead's allegation that there was inadequate clarification or qualification of the broad claim of 'reduce potential associated toxicities' due to, *inter alia*, the prominence of the claim on pages 3 and 4 of the leavepiece, the unqualified use of 'toxicities' as distinct from 'safety', the all-encompassing title which implied that a number of safety (toxicity) issues could be avoided, an imbalance in the prominence of the rates of neuropsychiatric toxicity observed with Juluca and the characterisation of these rates in the statement 'few drug-related AEs resulted in discontinuation'.

With regard to the comments regarding psychiatric adverse events, the Panel noted ViiV's submission that the rate was stated in the leavepiece as 'psychiatric disorders (12%)'. The Panel noted ViiV's submission that the discontinuations due to medicine-related adverse events was clearly stated as being 3%, so readers were in no doubt what was meant by 'few', and that only 1% of these

were due to psychiatric disorders. The Panel noted that the leavepiece stated that 4% of the Juluca group discontinued due to drug-related adverse events; there was no mention of how many subjects withdrew due to drug-related psychiatric adverse events. The Panel considered that the use of the word 'few' in relation to 4% was not unreasonable.

The Panel noted ViiV's submission that it refuted the allegation that the claim in question was too broad or all-encompassing as it specifically highlighted that the potential associated toxicities referred to were bone and lipid changes. The Panel noted its comments above, and at Point A. In the Panel's view, it was not clear in the leavepiece that 'toxicities' referred to only bone and lipid changes given that the same section of the leavepiece featured information on other adverse events including, *inter alia*, psychiatric disorders and diarrhoea.

Furthermore, the Panel disagreed with ViiV's submission that the neutral effect on serum lipids in the dolutegravir/rilpivirine group could be considered as reduction in toxicity.

Noting its comments above including at Point A, in the Panel's view, the implication that a two-medicine regimen reduced potential associated toxicities versus a three-medicine regimen in the claim 'Juluca- reduce your patients' ARV exposure & potential associated toxicities' was ambiguous, unsubstantiated, did not reflect the available information about adverse events, and was a misleading comparison. Breaches of Clauses 7.2, 7.3, 7.4 and 7.9 were ruled.

**ViiV exchange website**

The Panel noted that it was difficult from the materials provided to ascertain the different ways a user might navigate the website and therefore the order in which information would likely be read. The Panel noted that the statement 'Juluca-reduce your patients' ARV exposure & potential associated toxicities' appeared on a page which solely discussed bone health. From the screen shots provided, the previous page appeared to feature information regarding rates of virological failure vs continued triple therapy and the subsequent page featured information regarding lipid values and rates of adverse events from the SWORD studies. The Panel noted that there was a similar statement on another page titled 'Welcome to the 2-Drug Regimen Era', which stated 'Streamlining therapy to 2 drugs following suppression can reduce ARV exposure and potential associated toxicities'; however, that specific statement was not identified by Gilead and therefore not considered by the Panel.

The Panel noted that the claim at issue 'Juluca-reduce your patients' ARV exposure & potential associated toxicities' appeared as a heading on the webpage in question directly above the statement, in smaller font, 'Juluca-statistically significant Recovery in Bone Mineral Density (Dexa Sub-Study)'. Beneath were two side-by-side graphs which showed the change in hip and lumbar bone mineral density (BMD) for Juluca versus continued triple therapy. Below the graphs were two bullet points with statements regarding the % improvement in hip and lumbar spine bone mineral density and the decrease in measured markers of bone turnover for Juluca compared with patients continuing a TDF-based regimen. A highlighted box at the bottom of the webpage featured the heading 'Switching to Juluca provides a robust option for maintaining virological suppression while preserving bone health' above what appeared to be two videos: bone health and HIV and the effect of dolutegravir/rilpivirine on BMD in the SWORD studies.

In relation to the claim 'Juluca-reduce your patients' ARV exposure …' the Panel noted its comments and rulings above at Point A which it considered applied here and ruled a breach of Clauses 7.2, 7.3 and 7.4.

In relation to the reduction in potential associated toxicities the Panel considered that its comments at Point A above and its comments above (Point B in relation to the similar claim in the leavepiece) were relevant. The Panel noted that the only information on the webpage in question was in relation to bone health and focussed on the DEXA sub-study. In the Panel's view, the use of the plural to toxicity in the claim in question might imply that the term was used in relation to other toxicities in addition to bone. Furthermore, the Panel noted that the Juluca SPC stated in relation to this sub-study that any beneficial effect on fracture rate was not studied.

The Panel considered that the word 'associated' implied that the claimed potential reduction in toxicities was as a direct result of the claimed reduced ARV exposure. However, the data presented on the page in relation to effects on bone compared Juluca to those continuing on a TDF based regimen. The Panel noted Gilead's submission that there was evidence that switching from a TDF-based therapy to a different triple-based therapy was also associated with significant improvements in bone markers. In the Panel's view, the page implied that a reduction in ARV exposure in general would result in a reduction in potential associated toxicities, such as the effects on bone, however, it appeared to the Panel that the nature of the medicines was an important factor. Noting its comments above, in the Panel's view, the claim 'Juluca-reduce your patients' ARV exposure and potential associated toxicities' with regard to reduced potential associated toxicities was ambiguous, unsubstantiated, did not reflect the available information about adverse events and was a misleading comparison of Juluca with triple therapy. Breaches of Clauses 7.2, 7.3, 7.4 and 7.9 were ruled.

**C '…streamline treatment and reduce ARV exposure for your virologically supressed HIV patients' (Journal detachable sleeve (ref VIIV/DTGRPV/0002/17b(1)c))**

The Panel noted that the journal detachable sleeve featured a picture of a large rucksack next to a bench and a man walking away from the bench holding a smaller rucksack. In large font was the statement 'Progress with less' and below this it stated, in smaller font, 'Look inside and discover how to streamline treatment and reduce ARV exposure for

your virologically suppressed HIV patients'. The Panel noted that this piece of material was withdrawn by ViiV during inter-company dialogue in relation to the claim 'Progress with less'. As the material was not withdrawn due to the claim in question regarding reduced ARV exposure, the case preparation manager decided that the complaint regarding the claim at issue in this material should proceed.

The Panel noted that the sleeve had limited information. The reference to reduction in ARV exposure was not set within any context. There was no reference to moving from a three-medicine regimen to a two-medicine regimen. The Panel noted that the claim at issue included 'streamline' and noted its comments on this point above at Point A. Notwithstanding these comments the Panel considered that the use of 'streamline' in the statement implied that there was a comparison being made with another type of treatment, although that treatment was not identified.

The Panel noted that the sleeve was associated with the advertisement published within the journal. However, the sleeve was a separate piece of material that needed to meet the requirements of the Code. The Panel noted its comments above at Point A and considered that the claim in question regarding '… reduce ARV exposure …' was ambiguous, unsubstantiated and a misleading comparison of Juluca with other HIV treatments. Breaches of Clauses 7.2, 7.3 and 7.4 were ruled accordingly.

**D 'A 2- drug regimen may reduce ARV exposure and potential associated toxicities' (Juluca Fast Facts – ViiV exchange website (ref UK/DTGRPV/0005/18))**

The Panel noted that the Juluca Fast Facts material was A4 in size and double-sided. One side included statements about Juluca and the reverse side included the brand logo, prescribing information and a list of references.

The material featured Juluca's indication and the claim 'The first 2-drug regimen in a single pill'. A picture of the pill with its dimensions and components was displayed along with the statement 'powered by dolutegravir at the core'. Below this was information regarding the design of the SWORD studies and a statement that bioequivalence between Juluca and dolutegravir 50mg plus rilpivirine 25mg had been demonstrated. The statement 'JULUCA – non-inferior to continued 3-drug regimens in maintaining virological suppression at 48 weeks' appeared in the middle of the page above results from the studies , including rates of adverse events, drug-related adverse events resulting in discontinuation and adverse events reported in ≥5% of subjects in the Juluca arm. To the right of this, and separated by a vertical line, was the claim in question 'A 2-drug regimen may reduce ARV exposure and potential associated toxicities', which was the statement at issue in the complaint. Directly below the claim was the number three with an arrow pointing to the number 2, followed by the statements '2 well-tolerated agents, in 1 pill', 'Statistically significant recovery in bone mineral density (DEXA sub-study)', 'Maintains lipid levels'. Further below and at the bottom of the page was information regarding key drug interactions and how to prescribe Juluca.

Turning to the claim at issue, 'a 2- drug regimen may reduce ARV exposure and potential associated toxicities', the Panel noted the difference to the other statements considered above at points A, B and C in relation to ARV exposure; it stated 'may' reduce ARV exposure. The Panel noted its comments at points A and B above and considered that the use of the word 'may' did not make the claim any less ambiguous. The Panel noted its comments above at Points A and B and ruled a breach of Clauses 7.2, 7.3 and 7.4.

In relation to the claim in question regarding reduction in potential associated toxicities, the Panel considered that it was not clear in the material what the term 'toxicities' related to. Whilst there was information on bone mineral density and lipid levels below the claim at issue, there was also information about adverse events including psychiatric disorders, nasopharyngitis, headache and diarrhoea to the left of it. In the Panel's view, in the context of this material, the term toxicities could imply any adverse event. The Panel noted its comments at Point B above in relation to lipids; in its view the neutral effect on serum lipids in the dolutegravir/rilpivirine group could not necessarily be considered a reduction in toxicity. The Panel further noted it comments at Point B above regarding the ViiV exchange website and the word 'associated'; it implied that the claimed potential reduction in toxicities was as a direct result of the claimed reduced ARV exposure. However, as previously noted above, it appeared to the Panel that the nature of the medicines in the regimen was a fundamental factor in relation to the effects on, *inter alia*, bone.

The Panel noted its comments at Point A above in relation to adverse events in the SWORD studies. In the Panel's view, the claim regarding reduction in potential associated toxicities could not be substantiated by the SWORD studies.

In the Panel's view, the implication in the claim 'a 2- drug regimen may reduce ARV exposure and potential associated toxicities' that a two-medicine regimen might reduce potential associated toxicities versus a three-medicine regimen was ambiguous, unsubstantiated, did not reflect the available information about adverse events and was a misleading comparison. Breaches of Clauses 7.2, 7.3, 7.4 and 7.9 were ruled.

**2 Progress with less**

Gilead complained about the following statements: 'For your virologically suppressed patients, PROGRESS WITH LESS (Juluca leavepiece (ref UK/DTGRPV/0006/18)) and 'PROGRESS WITH LESS' (Juluca advertisement (ref VIIV/DTGRPV/0002/17(1)a)).

ViiV agreed during inter-company dialogue with Gilead to withdraw a journal detachable sleeve (ref ViiV/DTGRPV/0002/17b(1)c) in relation to the statement 'progress with less' and therefore that material in relation to the claim 'Progress with less'

was not considered by the Panel. There was no evidence that ViiV had agreed to stop using the claim elsewhere and thus the complaint in relation to the above material proceeded in the usual way.

**COMPLAINT**

Gilead submitted that in the claims at issue 'less' was not defined, was a hanging comparison and the claim, on its own and in the context in which it was used, implied that switching to Juluca was 'progressive', or an 'upgrade' and that a 2- medicine combination represented progress over a standard triple therapy ARV regimen. This impression was misleading, ambiguous and not capable of substantiation. Further, it created an unbalanced view that there were no risks attached to taking 'less'. Gilead alleged breaches of Clauses 7.2, 7.3, 7.4 and 7.10.

In relation to substantiation, the clinical study data (the SWORD studies) supporting the marketing authorisation for Juluca showed only non-inferior efficacy to the comparator regimens and did so in a very specific setting, with more adverse events for the advertised two-medicine combination than the standard of care comparator.

**RESPONSE**

ViiV stated that Juluca was a new approach to treatment in HIV in two important aspects. Firstly, it comprised of only two ARVs rather than the standard three, and secondly it was only for use as a maintenance treatment, not for the initial suppression of the virus. Use of the phrase 'Progress with less' conveyed the message that the treatment journey had begun and the use of Juluca was not for initial therapy, but for maintenance treatment after at least six months of suppression. It also reflected the continual evolution of HIV treatment as progress, with Juluca being the first licensed two-medicine regimen to have shown non-inferiority to traditional three medicine regimens, and the first licensed 'maintenance-only' HIV treatment.

In both the leavepiece and the advertisement in question, the phrase was introduced with 'For your virologically suppressed patients' making it clear that Juluca was not for initial treatment, but for those already on their treatment journey. In the advertisement, the first bullet point immediately beneath 'Progress with less' was 'The first single-pill, 2-drug regimen powered by dolutegravir at the core' which made it clear to the target audience of HIV specialists that the 'less' referred to fewer ARVs than in any other complete regimen. The leavepiece had a large picture of the tablet making clear it contained only two ARVs and went into much greater detail about the SWORD studies reinforcing the fact that Juluca was a complete regimen that contained fewer ARVs than any other.

ViiV refuted Gilead's assertion that 'Progress with less' '... created an unbalanced view that there were no risks attached to taking 'less'. There was no implication that there were no side-effects or risks to using Juluca. The advertisement and leavepiece made it clear that efficacy was no better than traditional triple therapy, all of which had a well-recognized risk of failure and contained the prescribing information with all the requisite contraindications, precautions and side-effects. The leavepiece went into more detail discussing the virological non-response data and adverse events seen in the SWORD studies, and also contained the obligatory prescribing information. ViiV denied any breach of Clauses 7.2, 7.3, 7.4 and 7.10.

**PANEL RULING**

The Panel noted Gilead's allegation that two statements in two identified materials were in breach of the Code. The Panel considered that each statement in the context of each material identified by Gilead should be considered separately.

**A For your virologically suppressed patients, PROGRESS WITH LESS (Juluca leavepiece (ref UK/DTGRPV/0006/18))**

The Panel noted that the statement appeared on the front page of the A5 bi-folded leavepiece. 'Progress with less' was in large capital letters near the top of the leavepiece and directly above it, in smaller less prominent font, was the statement, 'For your virologically suppressed HIV patients'. Below the statement was a picture of a large rucksack next to a bench and a man walking away from the bench holding a smaller rucksack. Below the picture was the statement 'A new era of HIV treatment starts today'. At the bottom of the page was Juluca's logo, licensed indication and a picture of a tablet with 'dolutegravir' on the left and 'rilpivirine' on the right and the caveat that the tablet was not to exact size.

The Panel noted that Juluca was indicated in adults who had been virologically suppressed on a stable regimen for at least 6 months. The Panel noted that the licensed indication was difficult to read; the font size was small and dark green in colour, set against a light green background. However, the Panel considered that the claim at issue made it clear that Juluca was not for initial therapy.

The Panel noted Gilead's submission that 'less' was a hanging comparison. The Panel noted that although the page made it clear that Juluca was a two-medicine regimen, it was not made clear what Juluca was 'less' than. Only when the leavepiece was opened would the reader see information regarding the SWORD studies and that Juluca was compared to 3-drug regimens. In the Panel's view, the reader should not have to turn a page to see the qualification to a claim. This was particularly so when considering the main claim on the front page of a leavepiece.

The statement 'A new era of HIV treatment starts today', which featured below the picture, implied that there was a comparison being made between Juluca and another HIV treatment. In the Panel's view, it was not clear exactly which HIV treatment Juluca was been compared to in the claim 'Progress with less'. Furthermore, the term 'progress' when read in conjunction with the phrase 'new era' could imply

some level of improvement versus the comparator, which was not supported by the SWORD studies which showed non-inferiority of Juluca compared to continued triple therapy.

Noting its comment above, in the Panel's view the claim 'For your virologically suppressed patients, PROGRESS WITH LESS' was ambiguous, a misleading comparison of Juluca with other HIV treatment and was not capable of substantiation, as alleged, and breaches of Clauses 7.2, 7.3 and 7.4 were ruled.

The Panel noted Gilead's allegation that the claim created an unbalanced view that there were no risks attached to taking 'less'. The Panel noted that it was unclear what risks Gilead was referring to. The Panel noted ViiV's submission that there was no implication that there were no side-effects or risks to using Juluca and that the leavepiece made it clear that efficacy was no better than traditional triple therapy, all of which had a well-recognized risk of failure. The Panel considered that Gilead had not proved, on the balance of probabilities, that the claim in question created an unbalanced view that there were no risks to taking 'less' and ruled no breach of Clause 7.10.

**B 'PROGRESS WITH LESS' (Juluca advertisement (ref VIIV/DTGRPV/0002/17(1)a))**

The Panel noted that the journal advertisement had the same picture as described above at Point 2A. 'Progress with less' was in large capital letters near the top of the advertisement. Directly above it, in smaller less prominent font, was the statement, 'For your virologically suppressed HIV patients'. Below 'Progress with less' were two bullet points which stated, 'The first single-pill, 2-drug regimen powered by dolutegravir at the core' and 'Treatment non-inferior to traditional 3-drug regimens at maintaining virological suppression at 48 weeks'. The advertisement also featured Juluca's logo with the statement 'A new era of HIV treatment starts today'. Juluca's indication was stated along with the statement 'DTG [dolutegravir] 50 mg + RPV [rilpivirine] 25 mg (bioequivalent to JULUCA) used in SWORD studies'.

The Panel noted that, unlike the claim at Point 2A above, the bullet points qualified that 'less' was in relation to a 2 medicine-regimen versus a 3 medicine-regimen.

Whilst the Panel noted the differences between the advertisement in question and the claim in the leavepiece at Point 2A, the Panel still considered that the word 'progress' was ambiguous and misleading. The word could imply advancement of some sort and, in the Panel's view, the claim was a misleading and an unsubstantiated comparison of Juluca compared with triple therapy. Breaches of Clauses 7.2, 7.3 and 7.4 were ruled.

The Panel considered that Gilead had not proved, on the balance of probabilities, that the claim 'PROGRESS WITH LESS' created an unbalanced view that there were no risks to taking 'less' as alleged and no breach of Clause 7.10 was ruled.

**3 2 well-tolerated agents**

Gilead complained about the following claims: 'is now available with just 2 well tolerated agents' (Juluca leavepiece (ref UK/DTGRPV/0006/18)) and '2 well-tolerated agents, in 1 pill' (Juluca Fast Facts – ViiV exchange website (ref UK/DTGRPV/0005/18)).

**COMPLAINT**

Gilead alleged that the claims were misleading in breach of Clause 7.2 as they placed undue emphasis on the safety profile of the individual components of the Juluca two medicine regimen without clarifying the safety profile of the medicine being promoted.

Gilead submitted that claims about tolerability must be clear and unambiguous and characterised appropriately, must include the use of appropriate substantiating data in a balanced fashion, while also citing the most up-to-date information to support the claims, including reference to the most appropriate summary of product characteristics (SPC).

As identified above, the SWORD study demonstrated that more participants who switched to the Juluca two medicine regimen (17 (3%)) reported adverse events leading to withdrawal than did participants who took triple therapy (3 (<1%)).

Table 3 of Section 5.1 of the Juluca SPC outlined that nearly 6 times as many patients discontinued study/study medicine (Juluca) due to adverse event or death (n=17) vs comparator (n=3); this critical information was absent from the respective component SPCs referenced against this claim, which did not report the clinical experience of combining these individual agents. Table 14, Section K-18 of the DHHS March 2018 guidelines, a leading source of guidelines for the treatment of HIV, identified that nervous system/psychiatric effects were common with both rilpivirine and dolutegravir.

Therefore, it was critical for the intended audience to be able to assess the appropriate frequency of these adverse events when combining these agents in a 2 medicine regimen and they should always be directed to the most relevant up-to-date information – the Juluca SPC.

Gilead alleged that the claims were misleading in breach of Clause 7.2.

**RESPONSE**

ViiV did not consider that the claims were ambiguous, that they misled, or misrepresented the data as alleged; the company thus denied a breach of Clause 7.2. The SWORD 1 and 2 studies were themselves conducted using the separate licensed agent rilpivirine and dolutegravir as opposed to the fixed dose combination. Hence referring to the separate agents did not misrepresent the study or the data. Furthermore, the above materials all cited adverse event information; total numbers of adverse events; medicine related discontinuations and adverse events occurring in 5% or more of individuals reported in the SWORD studies.
ViiV stated that it had ensured that its promotional

material would not be inconsistent with the licence by reminding readers that Juluca, although a new product and new way of treating virologically suppressed patients, was comprised of two ARVs with which they were familiar. This was consistent with the Code which required that all claims were capable of substantiation and that references were supplied promptly if requested.

There was no 'undue emphasis' on the safety profile of individual components as these also reflected the Juluca SPC as Gilead acknowledged in inter-company dialogue on 8 August. Similarly, the authors of the SWORD 1 and 2 studies publication stated 'No new or signature drug-related adverse events were observed with this combined therapy that were not already recognised with the use of the individual components, and no increase was seen in overall frequency or severity of drug-related adverse events. This absence of additive adverse reactions was not surprising given the lack of drug interaction between dolutegravir and rilpivirine'.

Gilead acknowledged in inter-company dialogue that the nature and frequency of adverse events in Section 4.8, of the Juluca SPC was consistent with the SPCs of the individual components. Section 5.1 of an SPC provided contextualizing information about the studies on which the licence was based and would be taken in to account by the regulators when approving an SPC. Had the regulators considered that the information in the adverse event table of Section 4.8 should be amended to differentiate the Juluca adverse event profile from its components, they would have required those changes to be included in Section 4.8. Gilead asserted concerns over nervous system/psychiatric effects and a greater number of adverse events leading to withdrawal, but the EPAR made clear 'No relevant new safety concerns … were identified as a result of the special monitoring. The psychiatric AE profile (including depression and suicidality) for dolutegravir and rilpivirine was comparable to the known safety profile for the single entities' and 'Based on all safety data submitted it was reasonable to conclude that the safety profile of the combined administration of dolutegravir and rilpivirine seemed to be consistent with the established safety profiles and the current labelling of the single agents. No additional risks or safety issues were identified '. Thus, it appeared that when the data were fully interrogated by the regulators, they did not see the need to amend the Juluca SPC to differ from the individual components in terms of adverse events.

ViiV noted that all of the materials included the Juluca prescribing information as mandated which had the obligatory direction to the Juluca SPC for further information on side-effects. As such the material was not misleading and was in line with the Code. ViiV denied a breach of Clause 7.2.

**PANEL RULING**

The Panel noted Gilead's allegation that two statements in two identified materials were in breach of the Code. The Panel considered each statement in the context of the material identified by Gilead.

**A 'is now available with just 2 well tolerated agents' (Juluca leavepiece (ref UK/DTGRPV/0006/18))**

The Panel noted that the claim at issue appeared on the back page, which appeared to be the final page of the bi-folded A5 leavepiece. As noted above in Point 1 A, there were three statements, in numerical descending bullet points: 'Juluca is non-inferior to 3-drug regimens at maintaining virological suppression …', is now available with just 2-well-tolerated agents …', 'all in 1 small pill'.

The Panel noted Gilead's allegation that the claim placed undue emphasis on the safety profile of the individual components of Juluca without clarifying the safety profile of the medicine being promoted and that the audience should be directed to the Juluca SPC.

The Panel noted that the claim at issue 'is now available with just 2 well tolerated agents' was referenced to the dolutegravir and rilpivirine individual SPCs and not the Juluca SPC, however, the Juluca SPC was also included in the list of references.

The Panel noted that ViiV's submission quoted the European Public Assessment report and stated 'Based on all safety data submitted it is reasonable to conclude that the safety profile of the combined administration of DTG [dolutegravir] and RPV [rilpivirine] seems to be consistent with the established safety profiles and the current labelling of the single agents. No additional risks or safety issues were identified '.

The Panel noted ViiV's submission that the SWORD studies were conducted using the separate licensed agents, dolutegravir and rilpivirine, as opposed to the fixed dose combination and that the Juluca European Medicines Agency (EMA) licence was underpinned by the SWORD 1 and 2 studies.

The Panel noted that page 3 of the leavepiece detailed safety results from the SWORD studies including the rates of adverse events, drug-related adverse-events resulting in discontinuation (Juluca 4% vs continued 3-drug regimens <1%), and adverse events reported in ≥ 5% of subjects in the Juluca arm (psychiatric disorders 12%, nasopharyngitis 10%, headache 8% and diarrhoea 6%). Page 3 of the leavepiece also stated that in studies supporting Juluca, dolutegravir 50mg and rilpivirine 25mg were used and that bioequivalence with Juluca had been demonstrated. The Panel noted that nonetheless the claim should be capable of standing alone.

The Panel noted its comments above and did not consider that the claim at issue 'is now available with just 2 well tolerated agents' in the context of the leavepiece was misleading by virtue of the emphasis on the individual components without clarifying the safety profile of Juluca, as alleged. No breach of Clause 7.2 was ruled.

**B '2 well-tolerated agents, in 1 pill' (Juluca Fast Facts – ViiV exchange website (ref UK/DTGRPV/0005/18))**

The Panel noted its description of this material in Point 1D above. The Fast Facts sheet referred to the SWORD studies including: design, the rates of adverse events in the two treatment arms, rates of drug-related adverse events resulting in discontinuation, adverse events reported in ≥5% of subjects in the Juluca arm and that bioequivalence of Juluca to dolutegravir 50mg and rilpivirine 25mg had been demonstrated.

The Panel noted its comments above at Point 3A. The Panel did not consider that the claim '2 well-tolerated agents, in 1 pill' in the context of the material was misleading by virtue of the emphasis on the individual components without clarifying the safety profile of Juluca, as alleged. No breach of Clause 7.2 was ruled.

**4 Size of tablet claim**

Gilead complained about the claim 'All in 1 small pill' (Juluca leavepiece (ref UK/DTGRPV/0006/18)).

**COMPLAINT**

Gilead submitted that the claim was ambiguous as it did not clarify the actual dimensions of the Juluca tablet. Without this clarification Gilead also considered the claim was a hanging comparison, as it was unclear to the reader in comparison to what the tablet was considered small. Gilead alleged a breach of Clause 7.2.

**RESPONSE**

ViiV did not consider that the claim was a hanging comparison, and therefore it denied a breach of Clause 7.2. 'Smaller' or 'smallest' without qualification would be, but 'small' was not comparative but an objective statement of fact. The dimensions of Juluca (14 x 7mm) substantiated the claim of 'small' and, although no comparison was made in the material, it was the smallest complete single-pill HIV regimen. By any standards, ViiV believed Juluca was small even when compared with what would be regarded as 'small'; in a study looking at the most commonly prescribed paediatric medications and their sizes, the dimensions of Juluca were comparably on the smaller spectrum of medications available for children (Jacobson *et al* 2016).

**PANEL RULING**

The Panel noted that the claim at issue featured on the back page of the bi-folded A5 leavepiece. The Panel noted that the dimensions of Juluca, as stated in the SPC, were 14 x 7mm. The Panel noted ViiV's submission that Juluca was the smallest complete single-pill HIV regimen. The Panel further noted that ViiV referred to a study by Jacobson *et al* (2016) on the sizes of commonly prescribed paediatric medicines; ViiV submitted that Juluca was comparably on the smaller spectrum of medicines available for children. The Panel noted that Jacobson *et al* stated that common paediatric antibiotics ranged from 8 to 25mm in length, median 17mm. The Panel further noted that Juluca was indicated for use in adults only.

In the Panel's view, the description 'small' was somewhat subjective, however, the Panel did not consider that the claim was ambiguous by not stating the dimensions, as alleged. The audience was an important consideration and the Panel considered whether the description would be misleading to HIV physicians. Noting its comments above, the Panel did not consider that the claim 'All in one small pill' was a hanging comparison or that Gilead had proved, on the balance of probabilities, that the description would be misleading to the intended audience. No breach of Clause 7.2 was ruled.

**5 High standards**

**COMPLAINT**

Gilead submitted that, generally, in relation to all of the above issues, ViiV had failed to maintain high standards, in breach of Clause 9.1.

**RESPONSE**

Overall ViiV strongly disputed the alleged breaches and a breach of Clause 9.1.

**PANEL RULING**

The Panel noted its comments and rulings of breaches of the Code at Points 1 and 2 above. In the Panel's view, ViiV had failed to maintain high standards and a breach of Clause 9.1 was ruled.

**Complaint received** **7 September 2018**

**Case completed** **15 August 2019**

**CASE AUTH/3067/9/18**

# MEMBER OF THE PUBLIC v CHIESI

## Payments to a health professional and certification

**A complainant who described him/herself as a friend of a current Chiesi employee and stated that he/she worked in a similar, non-identical industry, complained about compliance procedures within Chiesi and also that the company provided excessive hospitality to a named professor.**

**The complainant understood that the Code required all standard operating procedures (SOPs) to be up-to-date and alleged that Chiesi staff ignored the SOPs that had been written, no one took ownership of them and most were out-of-date.**

**The complainant also alleged that Chiesi paid over and above the 'reasonable amount' allowed for hospitality under the Code. The example given was that it paid one named medical professor substantial sums of money and for him/her to fly business class whenever he/she attended conferences on the company's behalf.**

**The complainant further identified the company employee who had allegedly used the Zinc stamp incorrectly; the stamp should only have been used by its owner, the medical director. The stamp was incorrectly used on marketing material which was then published.**

**The detailed response from Chiesi is given below.**

**The Panel noted that according to Chiesi the named professor had travelled eighteen times at the behest of Chiesi since 1 August 2016; each time as a consultant to the company rather than a delegate. The Panel noted that the professor appeared to have travelled in premium economy for the outward journey and in business on the return journey on two separate occasions when traveling to the USA and in business class on the outward and return journey when traveling to two long haul destinations.**

**The Panel noted that the complainant bore the burden of proof and had to establish his/her case on the balance of probabilities. A judgement had to be made based on the available evidence. The Panel did not consider that the complainant had established, on the balance of probabilities, that Chiesi had provided excessive hospitality in relation to the provision of inappropriate business class flights to the named professor as alleged. No breach was ruled in that regard. The Panel did not consider that the complainant had established that Chiesi's payments and expenses to the professor were excessive or inappropriate as alleged. The company had not failed to maintain high standards and no breach was ruled. The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such use and no breach of Clause 2 was ruled.**

**The Panel did not consider that the complainant had established that the employee in question had used the medical director's stamp to approve material in order to have it signed off as alleged. Based on the narrow allegation, the Panel ruled no breaches of the Code including Clause 2.**

**The Panel noted that the complainant had provided no evidence in support of his/her allegation that no one at Chiesi took ownership of its standard operating procedures (SOPs), and that most were out-of-date and were ignored by staff.**

**The Panel was concerned to note that ten SOPs were being updated after their review date, including SOPs covering high risk activities such as the procedure for the development, approval and use of press and media activities and material and the procedure for healthcare professional's attendance at third party organised meetings in the UK and overseas. The Panel further noted that an SOP related to the subject matter of the complaint, use of consultants and speakers, was being updated. The Panel noted that all but two of the ten SOPs had effective dates of 2014. The review dates ran from 31 December 2016 to 18 November 2018. The Panel noted Chiesi's submission that those ten SOPs had been assessed as still being compliant with both the 2016 and 2019 Codes and did not pose a risk to patient safety. The Panel had not been provided with these SOPs. The Panel was concerned that the owners of the ten SOPs which had not been updated had apparently not actioned reviews prior to the review dates as required by the relevant SOP.**

**The Panel considered that the failure to review and, if necessary, update SOPs promptly on or before their review dates as required by an SOP gave a poor impression to staff about the importance of SOPs and compliance and might have exposed the company to compliance risk. The Panel considered that Chiesi had failed to maintain high standards in this regard and a breach was ruled.**

**The Panel noted the summary of adverse findings, and the corrective and preventative action taken. In the Panel's view, the complainant had not established that staff were routinely not complying with or ignoring the company's SOPs as alleged and no breach was ruled in that regard.**

**The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such use and ruled accordingly.**

A complainant who described his/herself as a friend of a current Chiesi employee stated that he/she worked in a similar, non-identical industry,

complained about compliance procedures within Chiesi and also that the company provided excessive hospitality to a named professor.

**COMPLAINT**

The complainant stated that he/she understood that the Code required all standard operating procedures (SOPs) to be up-to-date and alleged that Chiesi staff ignored the SOPs that had been written, no one took ownership of them and most were out-of-date.

The complainant also alleged that Chiesi paid over and above the 'reasonable amount' allowed for hospitality under the Code. The example given was that it paid one named professor substantial sums of money and for him/her to fly business class whenever he/she attended conferences on the company's behalf.

In response to a request for further information, the complainant alleged breaches of the following:

Clause 22.1 for paying the named medical professor more than the amount allowed under the Code. The complainant alleged that this was not a one off, rather the professor in question was Chiesi's preferred delegate so the company bent the rules with regards to him/her. The complainant advised the Authority to seek the list of payments made to the professor over the years.

Clause 4 – compliance with SOPs. The complainant alleged that Chiesi put SOPs in place just for the sake of it, they were not followed, were largely out-of-date with many deviations and no one took ownership. The complainant submitted that the Authority might wish to get a list of the deviations.

The complainant submitted that he/she was unsure which clause to cite with regard to his/her allegation that the formal advertising approval stamp (used to approve copy on Zinc) should only be used by Chiesi's medical director/other approved people within the company (in line with the SOP) but was recently used by another named employee to approve material in order to get it signed off.

Clause 2 because the above brought the industry in to disrepute.

Clause 9 because Chiesi had failed to maintain high standards.

In response to a further request for more information, the complainant submitted that the professor's payments and expenses (including business class flights) were covered by way of several contracts between him/her and Chiesi. The complainant referred to internal swirl regarding whether it would be acceptable to pay for the professor's business class flights and noted guidance in the Code allowed for the individual to pay for an upgrade and that the company might pay for this for travel over 6 hours but the Code suggested premium economy.

The complainant further identified the company employee who had allegedly used the Zinc stamp incorrectly; the stamp should only have been used by its owner, the medical director. The stamp was incorrectly used on marketing material which was then published. The complainant alleged a breach of Clause 14.

When writing to Chiesi to advise it of the complaint, the Authority requested that it consider the requirements of Clause 2, 9.1, 14.1 and 22.1 of the Code.

**RESPONSE**

Chiesi submitted that it took all matters related to alleged breaches of the Code very seriously and had undertaken a thorough investigation.

In response to the alleged breach of Clause 22.1 Chiesi provided details of all flights which the professor had taken, at the behest of Chiesi, since 1 August 2016. There were four business class flights in the period in question, and on each occasion the professor acted as consultant to Chiesi and so business class travel was deemed appropriate.

Chiesi noted that the supplementary information to Clause 22.1 stated that companies should only offer or provide economy air travel to delegates sponsored to attend meetings, unless a flight was scheduled to take longer than six hours in which case companies might pay for an upgrade to premium economy or similar. As for consultants, the payment or reasonable honoraria and reimbursement of out of pocket expenses, including travel, was permissible. Given the requirements of Clause 22.1, the company did not consider that there had been a breach.

In response to the alleged breach of Clause 14.1, Chiesi submitted that the person alleged to have used the copy approval stamp was one of its managers. The person in question was not a listed signatory with the PMCPA or the Medicines and Healthcare products Regulatory Agency (MHRA) and thus was not authorised to approve material and did not certify any material as alleged.

Chiesi provided a copy of its SOP which detailed approval of material together with a copy of the approved material which it considered was that referred to by the complainant. As the material in question required examination only, there was no certificate to demonstrate certification. Details were provided. The material was examined by the then medical director (authorised signatory).

The medical director examined the items before applying his/her approval stamp on 25 May 2018. No one else had access to this stamp or indeed the medical director's login details for Chiesi's approval system.

Whilst the material was examined and approved by the medical director, he/she was not physically in the office. The employee at issue therefore applied the medical director's digital signature in the knowledge that the final content had been approved and that, consequently, the medical director was happy that the material would be sent out in his/her name.

In the circumstances set out above, Chiesi did not consider that it had breached Clause 14.1.

Further, Chiesi submitted that investigations into the allegations and in light of the facts set out above, it was confident that there had been no breach of Clause 9.1. The company prided itself on its compliance culture and established high standards of compliance and it constantly sought new and improved ways to ensure these continued. By way of example it had, *inter alia* an internal audit programme implemented a new training regime for employees, contractors and third parties and routinely followed up on initiatives to preserve and enhance the profile of compliance within Chiesi.

Chiesi submitted that it had also recently reviewed all of its SOPs and, as expected, many went above and beyond the requirements of the Code in terms of compliance obligations.

Chiesi submitted that none of its actions had brought, or would bring, the industry into disrepute and in that regard, it denied a breach of Clause 2.

In response to a request for further information Chiesi submitted that it had undertaken a thorough investigation into all payments made to the professor in question since August 2016 including honoraria and expenses. Chiesi submitted that analysis of the payments showed that Chiesi engaged the professor on a range of projects at a certain hourly rate which was both within its agreed rate card for an international Key opinion leader and was also in line with the hourly rate as described as part of a retainer consultancy service contract between Chiesi and the professor. According to Chiesi this contract was in the process of being updated; the update was initiated on 10 January 2019 which preceded correspondence from the PMCPA dated 7 February 2019 which first raised the issue of payments. Chiesi explained that during its investigation it identified an inconsistency in terms of which activities were covered and logged against the retainer consultancy service contract, and which activities were covered by separate consultancy agreements which were bespoke to specific assignments. The inconsistency was assessed by Chiesi's signatories as not being in breach of the Code or a risk to patient safety, however the update to the retainer consultancy service contract aimed to address the inconsistency.

Chiesi submitted that during its analysis of the documentation regarding all payments, it uncovered an additional flight to Europe in December 2016 which was not captured in its initial response to the PMCPA. The flight was paid for by the professor and the cost re-claimed from Chiesi. Chiesi only became aware of this omission through its in-depth analysis of invoices; it was not picked up when the professor was asked to validate the list of flights taken before Chiesi's initial response was submitted. Chiesi was unable to establish the class of travel for this additional return flight from the available invoice but as the flight was associated with a consultancy activity and not meeting attendance as a delegate it was a reasonable payment as part of reimbursement of out of pocket expenses, including travel. Given the requirements of Clause 22.1, Chiesi did not believe there had been a breach of the Code including of Clauses 9.1 and 2.

With regard to the allegation that most of Chiesi's SOPs were out of date, Chiesi conducted a full investigation into the status of all of its SOPs. Chiesi submitted that in total it had 132 SOPs, of which 30 had been updated since September 2018 and 4 of those were beyond their review date when they were updated; none of the 4 were considered to be Code-related. Chiesi submitted that there were currently ten SOPs out-of-date; importantly those ten SOPs had been assessed by its signatories as still being compliant with both the 2016 and 2019 Codes and did not pose a risk to patient safety despite being beyond their review dates. All ten SOPs were currently under review and would be updated in due course as appropriate. Chiesi highlighted that the introduction of GDPR had created a delay in updating a number of SOPs to ensure that all activities were in line with the relevant legal requirements.

Whilst Chiesi noted that the Authority requested information only for SOPs which were relevant to the Code, it wanted to include all SOPs to demonstrate the fact that it had a comprehensive suite of SOPs covering many areas of its business and took the existence and review of and adherence to SOPs extremely seriously. Chiesi submitted that the detailed breakdown of the status of its SOPs fully supported its position that the allegation that most of its SOPs were out-of-date was incorrect. Chiesi provided SOP-0276 Production and Management of Standard Operating Procedures which was the SOP that covered its management of SOPs. In the circumstances set out above, Chiesi did not consider that there was a breach of either Clause 9.1 or 2.

With regard to the allegation that SOPs were not being followed, Chiesi submitted that it had a robust compliance culture which encompassed all aspect of its business. It had a comprehensive initial training course for all employees, and contract staff which involved training on key SOPs and there was a wider learning management system which required all new starters to read, understand and, in many cases, pass a validation in relation to SOPs. This process was repeated each time SOPs were amended or updated.

Chiesi submitted that it conducted audits on a quarterly basis to monitor and assess compliance against both its SOPs and the Code. It had, over the last 12 months, widened the scope and the frequency of audits conducted and would continue that approach throughout 2019. Chiesi provided the adverse findings and relevant outcomes from audits conducted which were germane to Code-related activities and which were undertaken in 2018 in the period leading up to and including the date of the complaint.

Chiesi noted that in some cases breaches of SOPs were identified but these were addressed by producing corrective and preventative action (CAPAs) which were then followed through to correct the behaviour in question and to seek to prevent a recurrence. Chiesi noted that it adopted a very risk

adverse approach insofar as the Code was concerned and therefore its SOPs were purposefully drafted to be more restrictive than the correlating Code provisions.

Chiesi explained that one of the audits it conducted identified a potential Code breach; one of its sales representatives was found to have sent a prescribing guidelines document to two health professionals. Chiesi conducted a thorough investigation into the matter and appropriate action was taken. After further deliberation at its Code Forum (a monthly meeting at which Directors directly concerned with the Code met to discuss any Code matters or queries, and review of the corrective actions, Chiesi concluded that it was not a matter which should be the subject of a voluntary admission.

Chiesi shared additional information to demonstrate how important compliance with the Code was to its entire business ethos. As described above, all new employees and contracted staff undertook a comprehensive initial training course on the Code and were required to pass a *bona fide* validation to confirm understanding. In order to ensure continued understanding and adherence to the Code Chiesi submitted that it also had the following initiatives in place:

- Quarterly PMCPA Code Case Reviews for head office employees, where a minimum of 4 recent Code cases were reviewed and discussed by all areas of the business. Cases were prepared (with assistance from the compliance team) and presented by employees from all areas of the business, rather than by the compliance team. Attendance and participation at these quarterly updates were mandatory for all staff whose role was related to the Code and have been in place since February 2013.

- Quarterly Compliance Champion Case Reviews, which aimed to replicate the Quarterly PMCPA Code Case Review with members of field-based teams often using cases related to field force teams. Attendance and participation at these quarterly updates were mandatory, and compliance champions were retrained on an annual basis.

- Compliance objective was included on all company employees' management by objective (MBOs). This initiative had been in place for more than 5 years.

- Monthly compliance newsletters, which were circulated to all employees to ensure that everyone had a monthly reminder as to the importance of compliance with the Code in all activities. Input into the compliance newsletter was encouraged across the business. This initiative had been in place since December 2017.

- Weekly legal and compliance 'clinics' which were intended to have protected time for any ad hoc queries related to legal and/or compliance matters. This initiative had been in place since 31 January 2019.

**PANEL RULING**

The Panel noted that the complainant referred to Chiesi paying over and above the reasonable amount allowed for hospitality for a named professor including paying for him/her to fly business class when attending conferences on Chiesi's behalf. The Panel noted that the complainant did not provide any evidence in support of his/her allegation with regards to excessive hospitality and provided no specific details other than referring to business class flights and payments and expenses. The Panel noted that the complainant bore the burden of proof and that complaints are judged on the evidence provided by both parties.

The Panel noted the supplementary information to Clause 22.1, meetings and hospitality, with regard to appropriate air travel for delegates. The Panel noted, however, that business class travel could be offered to those who had been engaged to chair or speak at a meeting on behalf of a company. In this regard, token consultancy arrangements must not be used to justify such travel.

The Panel noted that according to Chiesi the named professor had travelled eighteen times at the behest of Chiesi since 1 August 2016; each time as a consultant to the company rather than a delegate. The Panel noted that the professor appeared to have travelled in premium economy for the outward journey and in business on the return journey on two separate occasions when traveling to the USA and in business class on the outward and return journey when traveling to two long haul destinations. The Panel noted Chiesi's submission that it was unable to establish the class of the return flight to Italy as it was paid for by the professor and the cost reimbursed by Chiesi. All other flights were in economy.

The Panel noted that the complainant bore the burden of proof and had to establish his/her case on the balance of probabilities. A judgement had to be made based on the available evidence. The Panel did not consider that the complainant had established, on the balance of probabilities, that Chiesi had provided excessive hospitality in relation to the provision of inappropriate business class flights to the named professor as alleged. No breach of Clause 22.1 was ruled in that regard.

In the Panel's view, the complaint went beyond the provision of business class flights. The complainant referred to 'payments and expenses (including business class flights)' and stated that payments made to the health professional were 'more than the amount allowed under the Code'. The Panel noted that the complainant did not refer to Clause 23.1 which covered consultancy payments and neither was it raised by the case preparation manager. The Panel could therefore make no ruling with regard to Clause 23.1 but considered the matter in relation to Clause 9.1. The Panel noted its comments about the complaint and the burden of proof. The Panel did not consider that the complainant had established that Chiesi's payments and expenses to the professor were excessive or inappropriate as alleged and no

breach of Clause 9.1 was ruled.
The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such use and no breach of Clause 2 was ruled.

With regards to the complainant's allegation regarding the inappropriate sign-off of materials, the Panel noted Chiesi's submission that the material referred to by the complainant, did not require certification. According to Chiesi they were examined by the medical director who applied his/her approval stamp within the company's electronic approval system; no one else had access to the medical director's stamp or login details. The employee at issue then applied the medical director's digital signature to the material and sent them.

The Panel did not consider that the complainant had established that the employee in question had used the medical director's stamp to approve material in order to get it signed off as alleged. Based on the narrow allegation, the Panel ruled no breach of Clause 14.1 and subsequently no breach of Clauses 9.1 and 2.

The Panel noted that the complainant had provided no evidence in support of his/her allegation that no one at Chiesi took ownership of its standard operating procedures (SOPs), and that most were out-of-date and were ignored by staff.

The Panel noted that Chiesi had an SOP covering the production and control of standard operating procedures which stated that the business head was the ultimate owner of the document and that SOPs were to be formally reviewed within a three year period to ensure that they remained current and appropriate, or to determine whether they were still needed. The Panel noted Chiesi's submission that 30 of 132 SOPs had been updated since September 2018; of these only 4 SOPs, none of which were Code related, were beyond their review date when they were updated. The Panel was concerned to note that ten SOPs were being updated after their review date, including SOPs covering high risk activities such as the procedure for the development, approval and use of press and media activities and material and the procedure for healthcare professional's attendance at third party organised meetings in the UK and overseas. These SOPs had effective dates in February 2014 and November 2014 and review dates in February 2017 and November 2017, respectively. The Panel further noted that an SOP related to the subject matter of the complaint, use of consultants and speakers, was being updated and had a review date in October 2017. The Panel noted that all but two of the ten SOPs had effective dates of 2014. The review dates ran from December 2016 to November 2018. The Panel noted Chiesi's submission that those ten SOPs had been assessed by its signatories as still being compliant with both the 2016 and 2019 Codes and did not pose a risk to patient safety. The Panel had not been provided with these SOPs. The Panel was concerned that the owners of the ten SOPs which had not been updated had apparently not actioned reviews prior to the review dates as required by the relevant SOP.

The Panel considered that the failure to review and, if necessary, update SOPs promptly on or before their review dates as required by SOP 0276 gave a poor impression to staff about the importance of SOPs and compliance and might have exposed the company to compliance risk. The Panel considered that Chiesi had failed to maintain high standards in this regard and a breach of Clause 9.1 was ruled.

The Panel noted the summary of Chiesi's audit adverse findings, and the corrective and preventative action taken. In the Panel's view, the complainant had not established that staff were routinely not complying with or ignoring the company's SOPs as alleged and no breach of Clause 9.1 was ruled in that regard.

The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such use and ruled accordingly.

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| **Complaint received** | **25 September 2018** |
| **Case completed** | **3 May 2019** |

CASE AUTH/3109/10/18

# COMPLAINANT v ASTRAZENECA

## AstraZeneca website

**A complainant who described him/herself as a concerned UK health professional, complained about a number of companies' websites including that of AstraZeneca UK. The pages at issue concerned Forxiga (dapagliflozin), Onglyza (saxagliptin) and Symbicort (budesonide/formoterol). Forxiga and Onglyza were used in certain patients with type 2 diabetes mellitus and Symbicort was used in certain patients with asthma or chronic obstructive pulmonary disease (COPD).**

**The detailed response from AstraZeneca appears below.**

**1 Forxiga**

**The complainant alleged that significant space was given to weight loss and reduction in blood pressure on a Forxiga promotional website, and these were both unlicensed indications.**

**The Panel noted that Forxiga was used in certain adults with type 2 diabetes mellitus to improve glycaemic control. The indication wording in section 4.1 of the SPC referred to, *inter alia*, Section 5.1 which featured clinical study results which referred to weight and blood pressure reductions.**

**In that regard, the Panel considered that reference to weight and/or blood pressure reduction was not necessarily unacceptable as part of the promotion of Forxiga, however, context was important. In the Panel's view, any references to weight and/or blood pressure reduction must be clearly set within the context of the primary reason to prescribe Forxiga ie to improve glycaemic control.**

**The Panel noted that each section of the website where weight or blood pressure reductions with Forixga were referred to, stated in bold font that Forxiga was not indicated for weight loss or the management of high blood pressure. There were also references in these sections to weight change being a secondary endpoint in clinical trials. It appeared to the Panel that information with regard to weight and blood pressure was displayed directly after the $HbA_{1c}$ data in the relevant sections, with the exception of the 'Pooled Data' section where weight reduction was presented alongside $HbA_{1c}$ data.**

**In relation to the website as a whole, given the context within which the information on weight and blood pressure reductions appeared, the Panel did not consider that the information was presented in such a way as to suggest that it was the primary reason to prescribe Forxiga.**

**On balance, the information on weight and blood pressure reduction for Forxiga in the context of the website in question did not amount to the promotion of unauthorized indications as alleged and the Panel ruled no breaches of the Code.**

**2 Onglyza**

**The complainant highlighted a claim and alleged that the difference in $HbA_{1c}$ reduction from baseline between Onglyza and sulphonylurea had been misrepresented.**

**The Panel noted that Goke *et al* stated that the mean changes from baseline $HbA_{1c}$ were -0.74% vs. -0.80% with Onglyza vs glipizide [sulphonylurea], respectively. The Panel considered the layout of the graphic and the immediate impression to a health professional. The Panel noted that -0.74% was in much larger font relative to the rest of the graphic and it appeared directly below the wording 'Onglyza vs SU [sulphonylurea]'. In addition, the information in the text box below compared the number of hypoglycaemic events over two years between Onglyza and an SU.**

**In the Panel's view, the immediate impression was that -0.74% was the difference between Onglyza and sulphonylurea in change in $HbA_{1c}$ from baseline, which was not so, and in that regard, it was a misleading comparison of the two medicines. The reference to the between-group difference, 0.06%, in very small font, was not sufficiently prominent and therefore did not negate the immediate misleading impression. Breaches of the Code were ruled including that AstraZeneca had failed to maintain high standards.**

**3 Symbicort**

**a) Use in COPD**

**The complainant alleged that exacerbations and symptom control had the relative rates of reduction displayed far more prominently than the absolute rate or indeed the co-primary endpoint that was not significantly different. The complainant also alleged that by stating that symptom control improved by 83%, AstraZeneca appeared to have intentionally ignored the non-significant endpoint of the study.**

**With regard to the exacerbation reduction webpage, in the Panel's view, the mention of the non-statistically significant co-primary result (FEV1) was disproportionate to the prominent representation of the co-primary result that showed statistical significance (number of severe exacerbations). The severe exacerbation rates with Symbicort Turbohaler vs formoterol (1.42 vs 1.84 per patient per year) were less prominently displayed than the relative risk reduction claim of 23%.**

**In the Panel's view, if relative risk reduction is stated, the absolute risk reduction should be presented**

**together with the relative risk reduction in such a way as to allow the reader to make an immediate assessment of the clinical impact of an outcome.**

**In the Panel's view, the 23% relative risk reduction in severe exacerbations for Symbicort Turbohaler vs formoterol was designed to be the primary take home message. The webpage highlighted, and placed disproportionate emphasis on, the relative risk reduction for one of the co-primary endpoints that had favoured AstraZeneca's product, without sufficient balance, and, in that regard, the immediate impression given by the webpage was a misleading comparison of Symbicort Turbohaler vs formoterol. Breaches of the Code were ruled including that AstraZeneca had failed to maintain high standards.**

**With regard to the symptom control webpage, the Panel noted that the primary endpoint of the study, PEF 5 minutes post-morning dose, was stated with a p-value of 0.603 which indicated that the difference observed between the two treatments was not statistically significant. The Panel noted that the main claim on the webpage related to a secondary endpoint, capacity of daily living (CDLM) score. The Panel considered that it was not unacceptable to present secondary endpoint data, as long as it was presented in the context of the primary endpoint results and with proportionate emphasis.**

**The Panel noted that the mean absolute change in CDLM score from baseline for both Symbicort Turbohaler and salmeterol/fluticasone (0.22 and 0.12, respectively) was mentioned on the webpage at issue, as was the difference between treatments of 0.10. The Panel noted the study authors' caution that, although statistically significant, the observed mean difference between treatments on this CDLM measure (0.10) was below the minimal important difference of 0.20.**

**In the Panel's view, the 83% relative improvement in total mean CDLM score for Symbicort Turbohaler vs salmeterol/fluticasone was designed to be the primary take home message. The webpage highlighted, and placed disproportionate emphasis on, the relative improvement of a secondary endpoint which favoured Symbicort Turbohaler, without sufficient balance, and, in that regard, the immediate impression given by the webpage was a misleading comparison of Symbicort Turbohaler vs salmeterol/fluticasone. Breaches of the Code were ruled including that AstraZeneca had failed to maintain high standards.**

**b) Use in asthma**

**The complainant alleged that the claim of a 39% reduction in exacerbations was not clear about what the absolute levels were; the seven times improvement in symptom control was again much more prominent than the absolute values and it was much harder to see that this was vs baseline and not vs alternate therapy.**

**With regard to exacerbation reduction, the Panel considered that there was no allegation with regard to the prominence of relative risk in relation to absolute risk. The Panel noted AstraZeneca's submission that the absolute figures for the claim in question were stated on the webpage. Based on the very narrow allegation the Panel ruled no breach of the Code.**

With regard to symptom control, the Panel considered that it was sufficiently clear that the claim '7x more asthma control days vs baseline' was versus baseline and not versus the comparator arm and ruled no breaches of the Code in that regard.

The Panel noted that the % of asthma control days at baseline and following treatment were stated for both Symbicort SMART and salmeterol/fluticasone + SABA, with a statement that the result was similar between the two groups. The Panel noted that the claim of 7x more asthma control days was versus baseline and therefore it was not a claim of relative improvement vs a comparator medicine as alleged. Based on the narrow allegation it considered that the claim at issue was not misleading and ruled no breaches of the Code.

A complainant who described him/herself as a concerned UK health professional, complained about a number of companies' websites including that of AstraZeneca UK Limited. The pages at issue concerned claims about Forxiga (dapagliflozin), Onglyza (saxagliptin) and Symbicort (budesonide/formoterol). Forxiga and Onglyza were used in certain patients with type 2 diabetes mellitus and Symbicort was used in certain patients with asthma or chronic obstructive pulmonary disease (COPD).

AstraZeneca stated that its UK medicines website was intended for UK health professionals and this was indicated to those who visited the website. The content of the website had been created with this intended audience in mind.

AstraZeneca did not believe the webpages at issue were in breach of the Code; it had however removed access to the pages whilst awaiting the Panel's rulings.

**1 Forxiga**

**COMPLAINT**

The complainant provided a web address (https//medicines.astrazeneca.co.uk/home/diabetes/forxiga.html) and alleged that although weight was stated to be a secondary endpoint and Forxiga was not indicated, there was significant space given on a promotional website to something that was not a licensed indication. The complainant did not consider that merely stating that this was not licensed meant that AstraZeneca was allowed to promote it. The same approach was taken with reductions in blood pressure. The complainant asserted that if AstraZeneca wanted to promote, it had to obtain a marketing authorization. The complainant noted that as AstraZeneca had previously been reprimanded for off-licence promotion, it appeared that whatever sanctions were imposed were insufficient.

When writing to AstraZeneca, the Authority asked it to consider the requirements of Clauses 2, 3.2 and

9.1. The Authority also advised AstraZeneca that, in its view, the reference to insufficient sanctions was a statement about sanctions and not an allegation that there had been a breach of undertaking.

**RESPONSE**

AstraZeneca submitted that the indication for Forxiga, ie glycaemic control in adults with type 2 diabetes, was clearly stated at the top of the webpage. Immediately after this was the dosing section followed by information on the dapagliflozin clinical trial data related to glycaemic control and $HbA_{1c}$ reduction. Three graphs depicted $HbA_{1c}$ control over several different studies to cover the breadth of clinical trial data and also long-term data on $HbA_{1c}$ control was presented.

Weight was an important consideration for diabetic patient management and was investigated as a secondary endpoint in the clinical development programme for dapagliflozin, since being established as a beneficial side effect of the medicine. The data was presented by baseline body mass index (BMI) and the subsequent weight loss in those groups compared with placebo from a randomised controlled trial. The reader, by clicking a relevant BMI group, was shown a graph representing the weight loss in that group over the time period of the study.

AstraZeneca submitted that the information was placed after the prominently displayed efficacy ($HbA_{1c}$) data and was clearly labelled as a secondary endpoint in the clinical trial. There was a prominent statement in a bold font stating that dapagliflozin was not indicated for weight loss. Blood pressure data was presented in a single chart following the weight loss data. Likewise, in this section, it was clearly stated that dapagliflozin was not indicated for blood pressure control. Cardiovascular indices (eg blood pressure) were important clinical considerations in the management of type 2 diabetics. As with weight loss, it had been established that similar to other sodium-glucose co-transporter 2 (SGLT2) inhibitors, dapagliflozin demonstrated a beneficial secondary benefit of blood pressure reduction.

In the weight loss and blood pressure sections, the reader was provided with a synopsis of the relevant clinical study, further allowing him/her to make an informed clinical decision.

AstraZeneca submitted that both the weight loss and blood pressure data had been provided in a considered manner, consistent with the data contained in the Forxiga summary of product characteristics (SPC). AstraZeneca denied that these sections of the website breached Clause 3.2; high standards had been maintained and as such there had been no discredit to, or reduction of, confidence in the pharmaceutical industry. AstraZeneca concluded that the material as approved for its intended purpose did not breach Clause 3.2 and thus it was also not in breach of Clauses 9.1 or 2.

Following a request for further information, AstraZeneca provided the full content of the Forxiga website.

**PANEL RULING**

The Panel noted that Clause 3.2 required that the promotion of a medicine must be in accordance with the terms of its marketing authorization and must not be inconsistent with the particulars listed in its SPC. The supplementary information to this Clause, 'Unauthorized indications', stated that the promotion of indications not covered by the marketing authorization for a medicine was prohibited.

The Panel noted that Forxiga was indicated in adults with type 2 diabetes mellitus to improve glycaemic control as either a monotherapy when diet and exercise alone did not provide adequate glycaemic control in patients for whom use of metformin was considered inappropriate due to intolerance, or in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, did not provide adequate glycaemic control. The indication wording in Section 4.1 of the SPC referred to, *inter alia*, Section 5.1. The Panel noted that Section 5.1, Pharmacodynamic properties, featured clinical study results which referred to weight and blood pressure reductions.

In that regard, the Panel considered that reference to weight and/or blood pressure reduction was not necessarily unacceptable as part of the promotion of Forxiga, however, context was important. In the Panel's view, any references to weight and/or blood pressure reduction must be clearly set within the context of the primary reason to prescribe Forxiga ie to improve glycaemic control.

The Panel noted that the Forxiga website in question featured, *inter alia*, information regarding Forxiga's licensed indications, dosing, clinical trial data, real world evidence, data vs saxagliptin and data in combination with glucagon-like peptide (GLP) or insulin.

The Panel noted that information relating to reductions in weight and/or blood pressure with Forxiga were present in multiple sections throughout the website, and not only in the 'Clinical Trial Data' section provided by AstraZeneca in its initial response. The Panel noted that self-regulation relied upon, *inter alia*, full and accurate responses from companies. The Panel was concerned that it was only after a request from the Panel that AstraZeneca provided the full website content which included information on weight reduction with Forxiga in the 'Real World Evidence', 'Pooled Data', 'Forxiga vs saxagliptin' and 'Forxiga in combination with GLP or insulin' sections of the website. There was also further information regarding blood pressure reduction with Forxiga in the 'Real World Evidence' section.

The Panel noted that in each section of the website above, where weight or blood pressure reductions with Forixga were referred to, it was stated in bold font that Forxiga was not indicated for weight loss or the management of high blood pressure. There were also references in these sections to weight change being a secondary endpoint in clinical trials. It appeared to the Panel that the information with regard

to weight and blood pressure was displayed directly after the $HbA_{1c}$ data in the relevant sections, with the exception of the 'Pooled Data' section where weight reduction was presented alongside $HbA_{1c}$ data.

In relation to the website as a whole, in the Panel's view, given the context within which the information on weight and blood pressure reductions appeared, the Panel did not consider that the information was presented in such a way as to suggest that it was the primary reason to prescribe Forxiga.

The Panel noted its comments above and considered that, on balance, the information on weight and blood pressure reduction for Forxiga in the context of the website in question did not amount to the promotion of unauthorized indications as alleged and no breach of Clause 3.2 was ruled. AstraZeneca had not failed to maintain high standards in this regard and no breach of Clause 9.1 was ruled. The Panel thus ruled no breach of Clause 2.

**2 Onglyza**

**COMPLAINT**

The complainant provided a web address (https//medicines.astrazeneca.co.uk/home/diabetes/onglyza.html) and noted that the claim regarding Onglyza vs sulphonylurea had a graphic indicating 0.74% which he/she assumed was the difference between the two as indicated in the title. However, in much smaller writing the complainant noticed that the difference was in fact 0.06%. The complainant thought that the difference had been misrepresented.

When writing to AstraZeneca, the Authority asked it to consider the requirements of Clauses 7.2, 7.3 and 9.1.

**RESPONSE**

AstraZeneca submitted that this section of the website was intended to address health professionals' questions about the comparison of sulphonylureas and dipeptidyl peptidase – 4 (DPP4) inhibitors such as Onglyza. AstraZeneca explained that it had been clinically well established and acknowledged by health professionals that DPP4 inhibitors were not as efficacious as sulphonylureas in terms of $HbA_{1c}$ reduction. However, health professionals were keen to know whether specific DPP4 inhibitors had comparable efficacy to sulphonylureas in this area and also demonstrated additional clinical relevant attributes (eg decreased incidence of hypoglycaemia).

With this in mind AstraZeneca noted that it had highlighted the reduction of $HbA_{1c}$ vs baseline achieved by Onglyza in a non-inferiority study vs a sulphonylurea (Goke *et al* 2010). This figure was close to that achieved by the sulphonylurea in the study and was declared non-inferior. The reader was then led through the sulphonylurea comparison data and finally invited to read details of hypoglycaemic events in the study.

All of the information was accurate and was provided in one place and was given due prominence.

AstraZeneca denied breaches of Clauses 7.2, 7.3 and 9.1.

**PANEL RULING**

The Panel noted that the webpage at issue was titled 'Onglyza vs SU [sulphonylurea]*'. Below this title was an arrow shaped highlighted box which stated in large font '-0.74% $HbA_{1c}$ reduction from baseline' and pointed to an adjacent second box, with a different background colour and smaller font, which stated ' … with Onglyza 5 mg at 1 year as add-on to metformin in a non-inferiority study vs a sulphonylurea (SU [glipizide mean dose 14.7 mg]) …vs -0.80%; between-group difference 0.06% (95% CI, -0.05% to 0.16%; n=858)[ referenced to Goke *et al* 2010]. Below the two boxes was a third highlighted box which stated '10 times fewer hypoglycaemic events……over 2 years with Onglyza vs an SU (3.5% of patients and 38.4% of patients, respectively)' [referenced to Goke *et al* 2013]. Below the boxes was the footnote to the title which stated '*Onglyza 5 mg + metformin was considered non-inferior to glipizide + metformin as the upper limit of the 95% confidence [sic] of the treatment difference in the per protocol (PP) analysis was <0.35 at 1 year. Mean baseline $HbA_{1c}$ of 7.5% for both groups. PP analysis: n=293 in each arm.'

The Panel noted the complainant's allegation that the difference in $HbA_{1c}$ reduction from baseline between Onglyza and sulphonylurea had, given the 'Onglyza vs SU' title, been misrepresented as it appeared from the graphic to be -0.74% but it was in fact 0.06%.

The Panel noted that Goke *et al* stated that the mean changes from baseline $HbA_{1c}$ were -0.74% vs. -0.80% with Onglyza vs glipizide [sulphonylurea], respectively. The Panel noted that the between-group difference of 0.06% was stated in the second box on the webpage at issue. The Panel considered the layout of the graphic and the immediate impression to a health professional. The Panel noted that -0.74% was in much larger font relative to the rest of the graphic and it appeared directly below the wording 'Onglyza vs SU'. In addition, the information in the text box below compared the number of hypoglycaemic events over 2 years between Onglyza and an SU. In the Panel's view, the immediate impression was that -0.74% was the difference between Onglyza and sulphonylurea in change in $HbA_{1c}$ from baseline, which was not so, and in that regard, it was a misleading comparison of the two medicines. The reference to the between-group difference, 0.06%, in very small font, was not sufficiently prominent and therefore did not negate the immediate misleading impression. A breach of Clauses 7.2 and 7.3 were ruled. The Panel considered that AstraZeneca had failed to maintain high standards and ruled a breach of Clause 9.1.

**3 Symbicort**

**b) Use in COPD**

**COMPLAINT**

The complainant provided a web address (https//medicines.astrazeneca.co.uk/home/respiratory/symbicort-copd.html) and noted that exacerbations and symptom control had the relative rates of

reduction displayed far more prominently than the absolute rate or indeed the co-primary endpoint that was not significantly different. The complainant alleged that by stating that symptom control improved by 83%, AstraZeneca appeared to have intentionally ignored the non-significant endpoint of the study.

When writing to AstraZeneca, the Authority asked it to consider the requirements of Clauses 7.2, 7.3 and 9.1.

**RESPONSE**

AstraZeneca submitted that this portion of the website focused on key clinical attributes that health professionals would consider in relation to prescribing a combination inhaler such as Symbicort for COPD patients. One key goal of COPD therapy was to reduce exacerbations. The relative risk reduction in exacerbations was a more informative clinical measure than absolute risk reduction in a comparative clinical study. However, both were needed by a health professional to gauge the clinical relevance of exacerbation outcome reduction in a given study.

AstraZeneca noted that information adjacent to the claim in question stated:

> 'This study demonstrated that Symbicort Turbohaler increased FEV1 (co-primary endpoint) by 1% vs formoterol (n=208 and n=201 respectively; p=NS) and demonstrated a reduction in severe exacerbations with Symbicort Turbohaler 200/6µg vs formoterol 6 µg: 1.42 vs 1.84 severe exacerbations per patient per year, respectively.'

AstraZeneca submitted that the statement provided the absolute values for severe exacerbation reduction, allowing the health professional to contextualise the prominent relative risk reduction. The absolute figures were stated as the number of exacerbations per patient per year (second co-primary endpoint) on the website in text above. The absolute figures were provided after the outcome of the first co-primary endpoint result, to ensure the figures were read in the context of that result. The statement disclosed the fact that the first of the two co-primary endpoints was not statistically different. The second co-primary endpoint was statistically significant. AstraZeneca submitted that the statistical outcome of the first co-primary endpoint not being significant did not impact the validity of the second more clinically relevant outcome.

AstraZeneca thus considered that the information presented would be neither ambiguous nor misleading to the intended audience of health professionals; the company denied a breach of Clauses 7.2, 7.3 and 9.1.

AstraZeneca noted that symptom control was another goal of COPD therapy. In this regard the information adjacent to the claim in question stated:

> 'The primary outcome of increase in morning PEF [peak expiratory flow] at 5mins post dose was similar (mean difference 1.0l/min, p=0.603) between Symbicort 400/12 µg bd vs salmeterol/fluticasone 50/500 µg bd. The increase in morning FEV1, at 15 mins was higher for Symbicort Turbohaler compared to salmeterol/fluticasone (0.14L vs 0.10L, p<0.05). A secondary outcome variable showed relative improvement in total mean CDLM [Capacity of Daily Living during the Morning] score with Symbicort Turbohaler 400/12 µg twice daily vs salmeterol/fluticasone 50/500 µg twice daily (0.22 vs 0.12 respectively; 95% CI 0.01-0.19, p<0.05) when measured from baseline.'

AstraZeneca submitted that the first sentence made clear that the primary outcome between the two study arms was similar and reported the non-significant p-value. The text made it clear to the reader that the improvement in total mean CDLM was a secondary endpoint and the results were mentioned after the results of the primary endpoint. With respect to the absolute figures, AstraZeneca did not agree with the complainant because the absolute figures were clearly stated. As stated above, it was important for health professionals to understand the effect of medicines on symptoms and exacerbations to help make an informed decision for the management of COPD patients. In both the sections above AstraZeneca noted that it had stated the more clinically relevant relative risk reduction allowing the reader to establish the difference between the treatment groups, this was followed by the result of the primary endpoints, absolute figures and confidence intervals, to provide context.

AstraZeneca did not consider that the information presented was ambiguous or misleading to the intended health professional audience. The company denied breaches of Clauses 7.2, 7.3 and 9.1.

**PANEL RULING**

The Panel noted that the website at issue featured a section titled 'COPD and Symbicort'. The Panel noted that the complainant had made allegations with regard to two webpages. One webpage was titled 'Exacerbation reduction' and the other was titled 'Symptom Control'. The Panel noted that the complainant was concerned that the relative rates of reduction were displayed far more prominently than the absolute rates on these pages and more prominently than the non-significant co-primary endpoint on the exacerbation reduction webpage, and that the 83% relative improvement claim on the symptom control webpage seemed to intentionally ignore the non-significant endpoint of the study.

The Panel noted that Clause 7.2 required that information, claims and comparisons must be accurate, balanced, fair, objective and unambiguous and must not mislead either directly or by implication, by distortion, exaggeration or undue emphasis. The Panel noted that the supplementary information to Clause 7.2 stated that referring only to relative risk, especially with regard to risk reduction, could make a medicine appear more effective than it was. In order to assess the clinical impact of an outcome, the reader also needed to know the absolute risk involved. In that regard relative risk should never be referred to without also referring to

the absolute risk. Absolute risk could be referred to in isolation.

**Exacerbation reduction webpage**

The Panel noted that below the 'Exacerbation reduction' title was the statement 'Symbicort Turbohaler reduced the incidence of severe exacerbations* by 23% vs formoterol' which was in bold font and referenced to Szafranski *et al* (2003). Below the statement, to the left, was a large red circle containing a downward pointed arrow with the text '23% relative risk reduction in severe exacerbations (p=0.043)'. The '23%' was in much larger font compared to the rest of the text on the webpage. To the right of this red circle in less prominent text it stated:

> 'This study demonstrated that Symbicort Turbohaler increased FEV1 (co-primary endpoint) by 1% vs formoterol (n=208 and n=201 respectively; p=NS) and demonstrated **a reduction in severe exacerbations*** with Symbicort Turbohaler 200/6 µg vs formoterol 6 µg: 1.42 vs 1.84 severe exacerbations* per patient per year, respectively' [referenced to Szafranski *et al* 2003].

Below the red circle, the Szafranski *et al* (2003) study design details were provided, including the statement, 'Primary efficacy variables: number of severe exacerbations* and FEV1' and a footnote in relation to the asterisk which defined severe exacerbations.

The Panel considered that, in principle, when a co-primary endpoint failed to achieve statistical significance it was not necessarily unacceptable to refer to other co-primary endpoint data so long as this was placed within the context of the overall study findings. The nature of the material might also be relevant.

The Panel noted that the study authors stated in their analysis that it was required that both primary variables should give statistical significance at the 5% level in order to keep the overall significance level to 5% in the final conclusion. In this regard, the Panel queried the prominence and weight given to one of the two co-primary endpoints.

In the Panel's view, the mention of the non-statistically significant co-primary result (FEV1) was disproportionate to the prominent representation of the co-primary result that showed statistical significance (number of severe exacerbations). The severe exacerbation rates with Symbicort Turbohaler vs formoterol (1.42 vs 1.84 per patient per year) were less prominently displayed than the relative risk reduction claim of 23%.

In the Panel's view, if relative risk reduction is stated, the absolute risk reduction should be presented together with the relative risk reduction in such a way as to allow the reader to make an immediate assessment of the clinical impact of an outcome.

The Panel considered the immediate impression to a busy health professional; in its view, the 23% relative risk reduction in severe exacerbations for Symbicort Turbohaler vs formoterol was designed to be the primary take home message of the webpage. The webpage highlighted, and placed disproportionate emphasis on, the relative risk reduction for one of the co-primary endpoints that had favoured AstraZeneca's product, without sufficient balance, and, in that regard, the immediate impression given by the webpage was a misleading comparison of Symbicort Turbohaler vs formoterol. A breach of Clauses 7.2 and 7.3 was ruled.

The Panel considered that AstraZeneca had failed to maintain high standards and ruled a breach of Clause 9.1.

**Symptom control webpage**

The Panel noted that below the 'Symptom control' title was the statement 'Change in lung function and morning activities: Symbicort Turbohaler vs salmeterol/fluticasone from baseline'. Below the statement, to the left, was a large red circle containing an upwards pointed arrow with the text '83% relative improvement in total mean CDLM score* (P<0.05)' [referenced to Partridge *et al* 2009]. The asterisks had a footnote with the definition of CDLM. The '83%' was in a much larger font compared to the rest of the text on the webpage. To the right of the red circle in less prominent text it stated:

> 'The primary outcome of increase in morning PEF at 5mins post dose was similar (mean difference 1.0L/min, p=0.603) between Symbicort 400/12 µg bd vs salmeterol/fluticasone 50/500 µg bd'.

Below this was the statement, 'The increase in morning FEV1 at 15 mins was higher for Symbicort Turbohaler compared to salmeterol/fluticasone (0.14L vs 0.10L, p<0.05)', followed below by:

> 'A secondary outcome variable showed **relative improvement in total mean CDLM* score** with Symbicort Turbohaler 400/12 µg twice daily vs salmeterol/fluticasone 50/500 µg twice daily (0.22 vs 0.12 respectively; 95% CI 0.01-0.19, p<0.05) when measured from baseline. Mean difference (0.10 [95% CI, 0.01-0.19; p<0.05]). A change of 0.2 units of CDLM represents the minimal important difference. The GCSQ [Global Chest Symptoms Questionnaire] score secondary outcome variable showed no significant difference in treatment arms' [referenced to Partridge *et al* 2009].

At the bottom of the webpage at issue were details about the study design.

The Panel noted that the primary endpoint of the study, PEF 5 minutes post-morning dose, was stated on the webpage with a p-value of 0.603 which indicated that the difference observed between the two treatments was not statistically significant. The Panel noted that the main claim on the webpage related to a secondary endpoint, CDLM score. The Panel considered that it was not unacceptable to present secondary endpoint data, as long as it was presented in the context of the primary endpoint

results and with proportionate emphasis.
The Panel noted that the mean absolute change in CDLM score from baseline for both Symbicort Turbohaler and salmeterol/fluticasone (0.22 and 0.12, respectively) was mentioned on the webpage at issue, as was the difference between treatments of 0.10. The Panel noted the study authors' caution that, although statistically significant, the observed mean difference between treatments on this CDLM measure (0.10) was below the minimal important difference of 0.20.

In the Panel's view, if relative improvement is stated, the absolute improvement should be presented together with the relative improvement in such a way as to allow the reader to make an immediate assessment of the clinical impact of an outcome.

The Panel considered the immediate impression to a busy health professional; in the Panel's view, the 83% relative improvement in total mean CDLM score for Symbicort Turbohaler vs salmeterol/fluticasone was designed to be the primary take home message of the webpage. The webpage highlighted, and placed disproportionate emphasis on, the relative improvement of a secondary endpoint which favoured Symbicort Turbohaler, without sufficient balance, and, in that regard, the immediate impression given by the webpage was a misleading comparison of Symbicort Turbohaler vs salmeterol/fluticasone. A breach of Clauses 7.2 and 7.3 was ruled.

The Panel considered that AstraZeneca had failed to maintain high standards in this regard and ruled a breach of Clause 9.1.

**b) Use in asthma**

**COMPLAINT**

The complainant provided a web address (https3// medicines.astrazeneca.co.uk/home/respiratory/ symbicort-asthma.html) and noted that the claim of a 39% reduction in exacerbations was not clear about what the absolute levels were; the seven times improvement in symptom control was again much more prominent than the absolute values and it was much harder to see that this was vs baseline and not vs alternate therapy.

When writing to AstraZeneca, the Authority asked it to consider the requirements of Clauses 7.2, 7.3 and 9.1.

**RESPONSE**

AstraZeneca noted that a statement adjacent to the claim in question read:

> 'The total number of severe exacerbations was 208 and 125 for salmeterol/fluticasone + SABA and Symbicort SMART, respectively.'

AstraZeneca submitted that the information initially described the results of the primary endpoint, and then led the reader onto information about the secondary endpoints. The absolute figures for this claim (a secondary endpoint) were therefore clearly stated alongside the claim in context of the results of the overall study.
AstraZeneca did not consider that the information presented was mbiguous or misleading to the intended audience; the company denied breaches of Clauses 7.2, 7.3 and 9.1.

With regard to the claim '7 x more asthma control days vs baseline', AstraZeneca noted that the absolute figures were clearly stated in the adjacent information ie:

> 'Compared with their baseline, patients who received Symbicort SMART 200/6µg bd + additional inhalations as needed had a seven-fold increase in asthma control days (5.8% vs 41.3%).'

AstraZeneca submitted that with respect to the allegation that it was difficult to see that the claim was vs baseline, the words 'vs baseline' were clearly stated in the visual which contained the claim ('7 x more asthma control days vs baseline'). It was reinforced in the text adjacent to the visual (stated above). In addition, the title above the visual for this claim stated: 'Symptom control Improvement in asthma control days', to ensure that there was no ambiguity that this was not a comparative claim with an alternative medicine.' Furthermore, the results for salmeterol/fluticasone vs baseline were also presented to ensure the reader had sufficient clinical information and context of the overall results for this endpoint.

AstraZeneca thus did not consider that the information presented was either ambiguous or misleading, and it denied breaches of Clauses 7.2, 7.3 and 9.1.

**PANEL RULING**

The Panel noted that the website at issue featured a section titled 'Asthma ICS/LABAs and Symbicort'. The Panel noted that the complainant had made allegations with regard to two webpages. One webpage was titled 'Exacerbation reduction' and the other was titled 'Symptom Control'.

Exacerbation reduction

The Panel noted that below the 'Exacerbation reduction' title was the statement 'Symbicort SMART reduced the incidence of severe asthma exacerbations** by 39% vs salmeterol/fluticasone + SABA' [referenced to Kuna *et al* (2007)]. Below the statement, to the left, was a large red circle containing a downwards arrow and the statement '39% fewer severe exacerbations** vs salmeterol/ fluticasone + SABA ($p<0.001$)'. The '39%' was in much larger font than the rest of the text on this webpage. To the right of the red circle in less prominent text it stated:

> 'Symbicort SMART prolonged the time to first severe exacerbation **(primary variable) vs fixed-dose salmeterol/fluticasone and Symbicort (33% reduction in hazard ratio p=0.003 and 26% reduction in hazard ratio p=0.026, respectively). There were no differences between treatments

in terms of mild exacerbations, lung function, asthma control days*** and asthma-related quality of life. Another secondary endpoint showed **fewer severe exacerbations**** with Symbicort SMART 200/6 µg bd + additional inhalations as needed vs salmeterol/fluticasone 50/250 µg bd + SABA as needed. Rate of severe exacerbation** events per 100 patients every 6 months was 19 for salmeterol/fluticasone + SABA and 12 for Symbicort SMART (p<0.001). The total number of severe exacerbations** was 208 and 125 for salmeterol/fluticasone + SABA and Symbicort SMART, respectively' [referenced to Kuna *et al* (2007)].

The Panel noted with regard to this webpage, the complainant stated that it was not clear what the absolute values were with regard to the claim of 39% reduction in severe exacerbations. The Panel considered that there was no allegation with regard to the prominence of relative risk in relation to absolute risk. The Panel noted AstraZeneca's submission that the absolute figures for the claim in question were stated on the webpage. Based on the very narrow allegation the Panel therefore ruled no breach of Clause 7.2.

**Symptom Control**

The Panel noted that below the 'Symptom control' title was the statement 'Improvement in asthma control days' [referenced to Kuna *et al* (2007)]. Below this statement, and to the left, was a large red circle with an upwards pointed arrow and the text, '7x more asthma control days vs baseline. Total number of asthma control days was another secondary endpoint'. The '7x' was in much larger font compared to the rest of the text on the webpage. To the right of the red circle in less prominent text it stated:

'Compared with their baseline, patients who received Symbicort SMART 200/6µg bd + additional inhalations as needed had a seven-fold increase in asthma control days (5.8% vs 41.3%). This was similar to the change in asthma control days seen with salmeterol/fluticasone 250µg bd + SABA (5.7% vs 43.7%).'

Below this text was the statement 'p value was not included in paper'.

The Panel noted that Kuna *et al* (2007) was a comparative study of Symbicort SMART versus, *inter alia*, salmeterol/fluticasone. For the secondary outcome variable of asthma-control days, the study authors stated that there was no statistical difference at the 5% level of significance between Symbicort SMART and salmeterol/fluticasone.

The Panel noted the text in the webpage at issue as set out above and considered that it was sufficiently clear that the claim '7x more asthma control days vs baseline' was versus baseline and not versus the comparator arm and ruled no breach of Clause 7.2 and 7.3 in that regard.

The Panel noted that the % of asthma control days at baseline and following treatment were stated for both Symbicort SMART and salmeterol/fluticasone + SABA, with a statement that the result was similar between the two groups. The Panel noted that the claim of 7x more asthma control days was versus baseline and therefore it was not a claim of relative improvement vs a comparator medicine as alleged. The Panel noted its comments above and based on the narrow allegation it considered that the claim at issue was not misleading by virtue of its prominence in this regard and ruled no breach of Clauses 7.2 and 7.3. The Panel therefore ruled no breach of Clause 9.1.

During its consideration of this case the Panel had a number of concerns about the webpages at issue and the completeness of AstraZeneca's response. The Panel provided further detail to AstraZeneca and requested that it be advised of its concerns and asked that the company review the webpages at issue bearing the above points in mind.

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| **Complaint received** | **29 October 2018** |
| **Case Completed** | **5 July 2019** |

**CASE AUTH/3112/11/18**

# COMPLAINANT v LILLY

## Rheumatology website

**A complainant who described him/herself as a concerned UK health professional complained about the Eli Lilly rheumatology website (www.lillyrheumatology.co.uk) stating that it was unclear whether the site was promotional or a resource for health professionals. On reaching the website the complainant confirmed that he/she was a health professional and initially the content appeared to focus on congresses and medical educational activities. However, under the 'our products' tab there was information on Olumiant (baricitinib) and Taltz (ixekizumab). There were no statements that this was a promotional site, and there was no link to prescribing information.**

**The complainant stated that Olumiant did not have a black triangle, although one was later evident on its own page. The complainant further alleged that on the 'our products' page Olumiant incorrectly had a grey triangle rather than a black one.**

**The complainant noted that throughout the website there were mechanisms to share links and content with others via email. The complainant referred to three examples and alleged that it was not clear to the recipient that the resultant email had been crafted by Lilly and led to a promotional website.**

**The complainant noted that the guidelines on how to use Lilly's twitter feed did not appear to have been updated since October 2016.**

**The detailed response from Lilly appears below.**

**With regard to the allegation that there was no statement to inform the user that the website was promotional, the Panel noted that the first page of the site following confirmation of the user as a UK health professional was the homepage which, *inter alia*, invited the reader to view highlights of a scientific conference in the education centre and a rheumatoid arthritis survey in the 'Our Projects' section. The Panel noted that the top of the webpage featured the Lilly logo and the tabs 'Home', 'About Lilly', 'Our projects', 'Our products', 'Education Centre' and 'Contact Us'. The Panel noted Lilly's submission that the website contained information about Lilly's products and was therefore promotional.**

**The Panel noted that the Code did not require promotional material to labelled as such, however, it must not be disguised and the identity of the responsible pharmaceutical company must be obvious from the outset. Context was important. The Panel considered that although the website contained a variety of information, including general disease information etc, it would, nonetheless, be sufficiently clear to health professionals who accessed this website that it was a Lilly website and that it was promotional. The Panel did not consider that the complainant had established, on the balance of probabilities, that the promotional nature of the website was disguised, and no breach of the Code was ruled.**

**The Panel noted Lilly's submission that if visitors clicked through to read about Lilly's products, every page had a prominent link to the prescribing information. Links to the summary of product characteristics (SPCs) and prescribing information for Olumiant and Taltz were included on the relevant pages of the 'Our Products' section of the website. The Panel considered that the links to the prescribing information in the 'Our Products' section met the requirements of the Code and ruled no breach was ruled.**

**The Panel noted that the complainant had not stated upon which webpage Olumiant did not have a black triangle. On digital material the Code required the black triangle symbol to be located adjacent to the first mention of the product as that was likely to be considered the most prominent display of the name of the product. The Panel considered that it was not possible to identify from the complaint, nor from Lilly's response, which mention of Olumiant on the website the complainant had referred to. The complainant bore the burden of proof and had not clearly identified the subject matter of the complaint. The Panel therefore ruled no breach of the Code.**

**The Panel noted the complainant's allegation that Olumiant did not have a black triangle but a grey one in the 'Our Products' pages. The complainant had not provided a screenshot of the webpage in question. In the Panel's view, based on the printed webpages provided by Lilly, the inverted triangle on the 'Our Products' pages did not appear grey as alleged and no breach of the Code was ruled in this regard.**

**With regard to the sharing content from the site with others via email, the Panel noted that in the three examples cited by the complainant the URL links from the emails in question referred to Lilly. However, an email about congress highlights made no mention of Lilly in the subject line nor in the email text. The Panel considered that it was not sufficiently clear to recipients of those emails that Lilly had created the email template for one health professional to send to another. In the Panel's view, Lilly's involvement in facilitating health professionals to share content from its rheumatology website would not be sufficiently clear to email recipients and it considered that Lilly had failed to maintain high standards in this regard. A breach of the Code was ruled.**

**The Panel noted Lilly' submission that the emails in question provided links to non-promotional content;**

**the company had, however, acknowledged that the website was a promotional website. The Panel noted Lilly's submission that recipients of the email who clicked on the links would first go to a self-declaration page before viewing any content. The Panel noted its comments above that promotional material did not need to be labelled as such, however, it must not be disguised, and the identity of the responsible pharmaceutical company must be obvious at the outset. The Panel noted that the self-declaration page featured the Lilly logo and referred to information for health professionals. In the Panel's view, the complainant had not proved, on the balance of probabilities, that the material accessed from the emails in question constituted disguised promotion and no breach of the Code was ruled.**

**With regard to the allegation that the guidelines on how to use Lilly's twitter feed had not been updated since 2016, the Panel noted Lilly's submission that the guidelines contained administrative instructions unrelated to any of Lilly's products. It was certified as a non-promotional item on first use to demonstrate that it had been through a rigorous approval process, however, Lilly considered that re-certification was not required by the Code.**

**The Panel noted that the Code required material which was still in use to be re-certified at intervals of no more than two years to ensure that it continued to conform with the relevant regulations relating to advertising and the Code. The twitter guidelines in question did not refer to a Lilly medicine. The Panel noted that the guidelines were certified on 1 November 2016 and that the complaint was received on 4 November 2018. The Panel noted Lilly's submission that the guidelines were accurate at the date of the complaint. Whilst the Panel was concerned about the ongoing oversight of the guidelines, it did not consider that the complainant had provided evidence that the guidelines constituted promotional material that required re-certification under the Code. No breach was ruled.**

A complainant who described him/herself as a concerned UK health professional complained about the Eli Lilly rheumatology website www.lillyrheumatology.co.uk.

**COMPLAINT**

The complainant stated that he/she was not sure if the website was a promotional website for Lilly's products or whether it was a resource for health professionals. On reaching the website at issue the complainant confirmed that he/she was a health professional. The website did not state it was promotional, and initially it appeared to focus on congresses and medical educational activities. However, under the 'our products' tab there was information for Lilly's two products Olumiant (baricitinib) and Taltz (ixekizumab). There were no statements that this was a promotional site, and there was no link visible to prescribing information.

The complainant stated that Olumiant did not have a black triangle, although one was later evident on its own page. The complainant further alleged that on the 'our products' page (https://www.lillyrheumatology.co.uk/ourproducts), Olumiant incorrectly had a grey triangle rather than a black one.

The complainant noted that throughout the website there were mechanisms to share links and content with others. For example, a link on a particular webpage created an email with the subject 'Discover Lilly Rheumatology on Social Media' with the content of the message 'Click this link to discover the value of social media in healthcare [link stated]'. Another webpage similarly created an email with the subject line 'Who is Lilly in Rheumatology?' and the content 'Click this link to find out more about Lilly's heritage [link stated]'. Further, the congress highlights page created an email that had the subject Congress Highlights with Click here to watch and download video highlights from the key rheumatology congresses [link stated]'. The complainant alleged that in none of these cases was it clear to the recipient that the email had been crafted by Lilly and was leading them to a promotional website.

The complainant noted that there were guidelines on how to use Lilly's twitter feed, but they were very old and did not appear to have been updated since October 2016.

When writing to Lilly, the Authority asked it to consider the requirements of Clauses 4.6, 4.10, 9.1, 12.1 and 14.5 of the Code.

**RESPONSE**

Lilly stated that its website contained a variety of content about rheumatoid arthritis, event highlights, Lilly's investment in the therapy area and its licensed medicines. It was very clear from the outset that this was a Lilly website that contained information about Lilly products and was therefore a promotional website. There was no restriction in the Code to providing high quality educational content in promotional material, and no requirement to label promotional material as such. Lilly did not accept that the material at issue breached Clauses 12.1 or 9.1 of the Code.

Lilly stated that to view the content, visitors had to self-certify that they were health professionals, otherwise they were directed to a section of the site suitable for members of the public. Every section of the website was presented transparently and no content was visible to readers until they had certified their status.

Lilly explained that if visitors clicked through to read about Lilly's products, every page of content had a prominent link to the prescribing information and to the relevant summary of product characteristics (SPC). Copies of downloaded pages were provided. Lilly submitted that the website complied with Clause 4.6.

Lilly stated that it took patient safety extremely seriously. A black triangle was included at the first and most prominent reference to the brand name on each content page as a reminder that the product

was subject to further monitoring. Lilly submitted that the position, size and colour of the triangle was consistent with the Code, and compliant with Clause 4.10.

Lilly submitted that the functionality on the website to email other health professionals with links to non-promotional content was presented as a simple tool for health professionals to use if they chose to. Clicking on the link generated a template email to be sent from one health professional to another. The recipient received an email from their colleague with a link. If he/she clicked on the link then (as a first time visitor to the website) they were taken to the self-declaration page before viewing any content. None of the email, the self-declaration page or the linked content were promotional or disguised.

Lilly stated that the Twitter user guidelines (copy provided) contained administrative instructions unrelated to any of Lilly's products, which it had certified as a non-promotional item on first use. This was done in order to record in Zinc that the guidelines had been through a rigorous approval process, and PMCPA guidance had recognised that companies' certification practices might go further than required by Clause 14 of the Code. The guidelines were accurate at the date of the complaint, and did not require recertification under the Code.

Following a request for further information, Lilly submitted that there was a prominent link to the SPC and prescribing information on the Taltz webpage (copy provided). Following a further request for information, Lilly supplied additional pages from the website at issue, including the homepage, the webpages that would generate the email templates referred to by the complainant, and content from the congress highlights webpages including the video transcripts.

**PANEL RULING**

The Panel noted that Clause 12.1 stated that promotional material and activities must not be disguised.

The Panel noted the complainant's allegation that the website initially appeared to focus on congresses and medical educational activities and there was no statement to inform the user that the website was promotional.

The Panel noted that, according to Lilly, before viewing website content, users would be presented with a self-declaration page featuring the Lilly logo. The self-declaration page had two options: information for UK health professionals, and information for patients prescribed Lilly rheumatology products/members of the public. The Panel noted that the first page of the site following confirmation of the user as a UK health professional was the homepage which referred, *inter alia*, to a named scientific conference and invited the reader to view highlights in the education centre, and a rheumatoid arthritis survey in the 'Our Projects' section. The Panel noted that the top of the webpage featured the Lilly logo and the tabs 'Home', 'About Lilly', 'Our projects', 'Our products', 'Education Centre' and 'Contact Us'. Lilly had submitted that the website in question contained information about Lilly's products and was therefore a promotional website.

The Panel noted that the Code did not require promotional material to labelled as such, however, it must not be disguised and the identity of the responsible pharmaceutical company must be obvious from the outset. Context was important. The website contained a variety of information, including, general disease information, Lilly's commitment to the therapy area, scientific conference activity and information on Lilly's medicines; the different sections of the website were labelled, and each section appeared to contain Lilly's logo. Noting its comments above, the Panel considered that it would be sufficiently clear to health professionals who accessed this website that it was a Lilly website and that it was promotional. The Panel did not consider that the complainant had established, on the balance of probabilities, that the promotional nature of the website was disguised, and no breach of Clause 12.1 was ruled.

The Panel noted the complainant's allegation that there was no visible link to prescribing information. Clause 4.6 required that promotional material on the internet must contain a clear prominent statement as to where the prescribing information can be found. Lilly submitted that should visitors click through to read about Lilly's products, every page of content had a prominent link to the prescribing information. The Panel noted that each Olumiant webpage in the 'Our Products' section contained links to the summary of product characteristics (SPC) and prescribing information and that the 'Our products' section included information about Taltz, including links to its SPC and prescribing information. The Panel considered that the links to the prescribing information in the 'Our Products' section met the requirements of the Code and ruled no breach of Clause 4.6.

The Panel noted the complainant's allegation 'Olumiant does not have a black triangle, although one is later evident on its own page'. It was not clear to the Panel from either party as to which webpage the complainant had referred. The Panel noted that Clause 4.10 stated that when required by the licensing authority, all promotional material must show an inverted black equilateral triangle to denote that additional monitoring was required in relation to adverse events. The supplementary information stated that for digital communications the black triangle symbol should be located adjacent to the first mention of the product as this was likely to be considered the most prominent display of the name of the product. As the complainant bore the burden of proof and had not clearly identified the subject matter of the complaint, the Panel ruled no breach of Clause 4.10.

The Panel noted the complainant's allegation that Olumiant did not have a black triangle but a grey one in the 'Our Products' pages. The complainant

had not provided a screenshot of the webpage in question. In the Panel's view, based on the printed webpages provided by Lilly, the inverted triangle on the 'Our Products' pages did not appear grey as alleged and no breach of Clause 4.10 was ruled in this regard.

The Panel noted the complainant's allegation that throughout the website there were mechanisms for users to share links and content with others. The Panel noted that the complainant referred to three examples and alleged that in none of these cases was it clear to the recipient that the email had been crafted by Lilly and was leading the reader to a promotional website.

The Panel noted Lilly's submission that the website provided functionality and aided a health professional to share content from the site with others. The congress highlights webpage featured an email icon with the text 'share by email'. The email template featured 'Congress Highlights' in the subject line and the body of the email stated 'Click here to watch and download video highlights from the key rheumatology congresses' with a URL link to the congress highlights section of the Lilly rheumatology website. The Panel noted that the 'Social Feeds' and 'Heritage' webpages in the 'About Lilly' section also featured email icons with the text 'share by email'. The email templates generated from these icons included the subject lines 'Who is Lilly in Rheumatology' and 'Discover Lilly Rheumatology on Social Media'. The content of the email templates stated: 'Click this link to find out more about Lilly's heritage' and 'Click this link to discover the value of social media in healthcare', respectively.

The Panel noted that the URL links from the emails in question referred to Lilly. However, the congress highlights email did not refer to Lilly in either the subject line or in the email text. The Panel considered that it was not sufficiently clear to recipients of those emails that Lilly had created the email template for one health professional to send to another. In the Panel's view, Lilly's involvement in facilitating health professionals to share content from its rheumatology website would not be sufficiently clear to email recipients and it considered that Lilly had failed to maintain high standards in this regard. A breach of Clause 9.1 was ruled.

The Panel noted Lilly' submission that the emails in question provided links to non-promotional content. In the Panel's view, whilst the webpages accessed from the URL links in question did not appear to mention a Lilly medicine, the Lilly Rheumatology website contained promotional content about Lilly medicines, and was therefore a promotional website, as acknowledged by Lilly. The Panel noted Lilly's submission that recipients of the email who clicked on the URL links would first go to a self-declaration page before viewing any content. The Panel noted its comments above that promotional material did not need to be labelled as such, however, it must not be disguised, and the identity of the responsible pharmaceutical company must be obvious at the outset. The self-declaration page featured the Lilly logo and referred to information for health professionals. In the Panel's view, the complainant had not proved, on the balance of probabilities, that the material accessed from the emails in question constituted disguised promotion and no breach of Clause 12.1 was ruled.

In response to the complainant's allegation that guidelines on how to use Lilly's Twitter feed did not appear to have been updated since 2016, Lilly had submitted that the guidelines contained administrative instructions unrelated to any of its products; it was certified as a non-promotional item on first use to demonstrate that it had been through a rigorous approval process, however, Lilly considered that re-certification was not required by the Code.

Clause 14.5 stated that material which was still in use must be re-certified at intervals of no more than two years to ensure that it continued to conform with the relevant regulations relating to advertising and the Code. The Panel noted that the Twitter guidelines in question did not refer to a Lilly medicine, however, there was information directed towards patients which requested them not to use Lilly's social media channels to report side effects; alternative channels for reporting side effects were provided. The terms and conditions stated, *inter alia*, '… please do not communicate with us on our medicines' and that Lilly reserved the right not to respond to communications that named any medicine. The Panel noted that the guidelines were certified on 1 November 2016 and that the complaint was received on 4 November 2018; Lilly had submitted that the guidelines were accurate at the date of the complaint. Whilst the Panel was concerned about the ongoing oversight of the guidelines, it did not consider that the complainant had provided evidence that the guidelines constituted promotional material that required re-certification under Clause 14.1 or educational material for the public or patients which related to diseases or medicines which required re-certification under Clause 14.3. In that regard, the Panel therefore ruled no breach of Clause 14.5.

**Complaint received** **4 November 2018**

**Case completed** **24 May 2019**

**CASE AUTH/3128/12/18**

# COMPLAINANT v JANSSEN

## Promotion of Imbruvica

**An individual complained about a leaflet promoting Imbruvica (ibrutinib) on Janssen-Cilag's exhibition stand at a meeting held in Glasgow in November 2018. The complainant alleged that the leaflet was misleading because it used the claim 'Destination survival' without any mention of survival data and it misleadingly implied that there was a survival benefit with Imbruvica which was not so.**

**Imbruvica was used in the treatment of chronic lymphocytic leukemia (CLL), relapsed or refractory mantle cell lymphoma (MCL) and Waldenström's macroglobulinaemia (WM).**

**The detailed response from Janssen is given below.**

**The Panel noted that the leaflet contained Imbruvica's logo with the strapline (claim) 'Destination survival' on multiple pages. The leaflet was titled, 'Getting started with once-daily, oral, single-agent Imbruvica (ibrutinib)'. The second page of the leaflet listed all of Imbruvica's indications and so, in the Panel's view, the leaflet and therefore the strapline 'Destination survival' might be considered in the context of all Imbruvica's indications.**

**The Panel considered that health professionals working in oncology would, on the balance of probabilities, associate the strapline 'Destination survival' with overall survival benefit.**

**The Panel noted Janssen's submission that data supporting ibrutinib's efficacy in improving overall survival in CLL was included in Section 5.1 of the SPC and published by Burger *et al* (2015) and Byrd *et al* (2014). Burger *et al* reported that ibrutinib resulted in significantly longer progression-free survival (primary endpoint) and significantly prolonged overall survival (secondary endpoint) vs chlorambucil in previously untreated CLL patients. Byrd *et al* stated that ibrutinib significantly improved progression-free survival (primary endpoint) and significantly improved overall survival (secondary endpoint) vs ofatumumab in previously treated CLL patients.**

**The Panel considered the body of clinical data provided by Janssen. The Panel noted that not all studies across all Imbruvica's licensed indications had demonstrated a statistically significant overall survival benefit vs the comparator arm. The Panel considered that as not all of Imbruvica's licensed indications had the body of evidence to support the claim 'Destination survival' which appeared as part of the Imbruvica logo and was included in the leaflet which featured all of Imbruvica's indications, the claim was misleading and incapable of substantiation and breaches of the Code were ruled. The Panel considered that Janssen had failed to maintain high standards in this regard and a further breach of the Code was ruled.**

**The Panel noted the complainant's allegation that the term 'Destination survival' in the leaflet was misleading in the absence of any survival data within the leaflet. The Panel noted Janssen's submission that the leaflet was intended as a user-friendly simplification of the prescribing information and contained no efficacy data. The Panel did not consider that the claim in question was misleading by virtue of the leaflet not containing survival data as alleged and, in that regard, it ruled no breach of the Code.**

An individual complained about information on Janssen-Cilag Limited's exhibition stand which promoted Imbruvica (ibrutinib) at a UK Oncology Nurses Society meeting in Glasgow in November 2018. Imbruvica was used in the treatment of chronic lymphocytic leukemia (CLL), relapsed or refractory Mantle cell lymphoma (MCL) and Waldenström's macroglobulinaemia (WM).

**COMPLAINT**

The complainant noted that a leaflet (ref PHGB/IBR/0616/0007(9)) on the Janssen stand stated 'Destination survival' (photographs provided). The leaflet did not mention survival, it only referred to: How to give the medicine; side-effects and their management; special populations; precautions for use and prescribing information.

The complainant alleged that the reason there was no mention in the leaflet of 'survival' was because there was no OS (overall survival) benefit with the medicine. Another leaflet stated PFS (progression free survival) benefit not OS benefit (there was no OS benefit with the medicine).

The complainant alleged it was misleading on Janssen's part to use the term 'Destination survival' without any mention of 'survival' data in the first leaflet and secondly, more importantly, as there was no OS benefit – this misled the reader of the first leaflet to think that there was a survival benefit with the medicine when there was none.

In writing to Janssen, attention was drawn to the requirements of Clauses 7.2, 7.4 and 9.1 of the Code.

**RESPONSE**

Janssen refuted the complainant's remarks that there was no OS benefit with the medicine and that the strapline 'Destination survival' was misleading. Janssen submitted that the leaflet was of a high standard (Clause 9.1) and met the requirements of Clauses 7.2 and 7.4.

Janssen submitted that the strapline 'Destination survival' accompanied the Imbruvica logo and referred to the strength of the efficacy data that

supported the pivotal registrational studies which demonstrated clinically significant survival outcomes. The data supporting ibrutinib's efficacy in improving overall survival (OS) in CLL was listed in Section 5.1 of the Imbruvica summary of product characteristics (SPC) for both patients with untreated CLL (first line therapy) as well as patients who had received at least one prior therapy (relapsed/ refractory patients) as detailed below.

For patients with untreated CLL, Janssen submitted that the marketing authorization application for ibrutinib was supported by a randomised, multi-centre, open-label phase 3 study (PCYC-1115-CA) in patients with treatment naïve CLL who were 65 years and older (n=269). Patients were required to have at least one co-morbidity that precluded the use of front-line chemo-immunotherapy with fludarabine, cyclophosphamide and rituximab. In this study, progression free survival (PFS), as assessed according to International Workshop on CLL (IWCLL) criteria, indicated an 84% statistically significant reduction in the risk of death or progression in the ibrutinib arm. Efficacy results for Study PCYC-1115-CA (Burger *et al*, 2014) were shown in Table 4 and the Kaplan-Meier curves for PFS and OS were shown in Figures 2 and 3, respectively of the SPC that demonstrated a survival benefit for patients treated with ibrutinib. Burger *et al* (2015) concluded that 'Ibrutinib was superior to chlorambucil in previously untreated patients with CLL or small lymphocytic lymphoma, as assessed by progression-free survival, overall survival, response rate, and improvement in hematologic variables'.

For patients with CLL who received at least one prior therapy, Jansen submitted that the marketing authorization for this patient cohort was supported by one uncontrolled study and one randomised, controlled study. The randomised multi-centre, open-label phase 3 study of ibrutinib vs ofatumumab (PCYC-1112-CA) was conducted in patients with relapsed or refractory CLL (n=391). Patients were randomised 1:1 to receive either ibrutinib until disease progression (or unacceptable toxicity) or ofatumumab. Fifty-seven patients randomised to ofatumumab crossed over following progression to receive ibrutinib. The median age of CLL patient was 67 years and the median time since diagnosis was 91 months. Progression free survival as assessed according to IWCLL criteria indicated a 78% statistically significant reduction in the risk of death or progression for patients in the ibrutinib arm. Analysis of OS demonstrated a 57% statistically significant reduction in the risk of death for patients in the ibrutinib arm. The authors of this pivotal study concluded that ibrutinib, as compared with ofatumumab, significantly improved progression-free survival, overall survival, and response rate among patients with previously treated CLL or small lymphocytic lymphoma (SLL) (Byrd *et al*, 2014).

Janssen submitted that the intent of the leaflet ('Getting started with once-daily, oral, single-agent' (ref PHGB/IBR/0616/0007(9)), specifically to guide UK health professionals commencing treatment in new patients, was to highlight the safety and appropriate use of ibrutinib:

- The NICE (National Institute for Health and Care Excellence) Technical Appraisal Guidance for ibrutinib use in CLL patients and guidance on which patients were eligible to receive ibrutinib
- How to administer ibrutinib – dosing adjustments, caution in special populations and drawing attention to potential drug interactions and precaution for use.

The guide was intended as a user-friendly simplification of the prescribing information to educate health professionals, and in particular, oncology nurses and pharmacists by guiding patients on the use of ibrutinib to treat their disease. Whilst each section page of the guide was introduced in the left-hand bottom corner with the strapline 'Destination Survival', at no point was any efficacy information or, specifically to this case, survival data listed within this guide and as such, capable of substantiation. The guide was referenced by the SPC that would contain all the distinct information for ibrutinib.

Janssen submitted that the complainant's assertation that 'there is no OS benefit' was incorrect as the pivotal studies outlined above demonstrated a survival benefit (PFS and OS). Janssen therefore submitted that the materials had maintained high standards (Clause 9.1) and that the strapline 'Destination survival' was accurate, balanced, fair and unambiguous (Clause 7.2) and capable of substantiation (Clause 7.4).

Janssen stated that the intent of the leaflet was to ensure therapy management of CLL for patients considered for ibrutinib and to inform prescribers about specific precautions as outlined in the prescribing information. Janssen refuted the complainant's suggestion that the guide had no survival data as the Code allowed for claims to be made about a product provided they could be substantiated. Janssen was confident that the efficacy data provided within the SPC Section 5.1 clearly substantiated the claim. Janssen therefore submitted that the strapline 'Destination survival' was accurate, balanced and objective and the materials used at the meeting were within the spirit and guidance of the Code.

Following a request for further information, Janssen provided additional survival data for further Imbruvica indications.

Janssen submitted that the safety and efficacy of Imbruvica in patients previously treated for CLL were further evaluated in a randomised, multicentre, double-blinded phase 3 study of Imbruvica in combination with bendamustine/rituximab (BR) vs placebo + BR (Study CLL3001-HELIOS STUDY). Patients (n=578) were randomised 1:1 to receive either Imbruvica 420mg daily or placebo in combination with BR until disease progression, or unacceptable toxicity. Progression free survival (PFS) was assessed according to IWCLL criteria. Efficacy results for Study CLL3001 were shown in the SPC (details provided). The HELIOS study was conducted in patients with relapsed/refractory CLL/ SLL and was the first trial to show a survival benefit with ibrutinib-based therapy vs a standard chemo-immunotherapy regimen, even in the context of

a crossover design. These results supported the continued use of ibrutinib, with maintenance of superior PFS and OS vs the placebo + BR arm and an increase in overall response rate and complete response rates over time. It was notable that longer-term follow-up revealed a significant improvement in survival for ibrutinib + BR-treated patients compared with placebo + BR, despite the possibility of crossover after progression.

For treatment of adults with relapsed or refractory mantle cell lymphoma (MCL), Janssen submitted that study PCYC-1104-CA was a multicentre, open-label phase 2 registration trial of ibrutinib (n=111) where the primary endpoint was the rate of overall response and secondary endpoints included survival efficacy outcomes such as PFS, OS and safety. The 24-month PFS and OS rates were 31% (95% confidence interval [CI], 22.3-40.4) and 47% (95% CI, 37.1-56.9), respectively. At a median follow up of 26.7 months, the median PFS was 13 months (95% CI: 7.0, 17.5 and the median OS was 22.5 months (95% CI: 13.7, not estimable). In study MCL3001 (RAY), Janssen submitted that median PFS survival was significantly improved in the ibrutinib group compared with the temsirolimus group (95% CI); Ibrutinib 14.6 months (10.4, not estimable) vs temsirolimus 6.2 months (4.2, 7.9) [HR = 0.43 [95% CI: 0.32, 0.58]]. After a median follow up for over three years, ibrutinib significantly prolonged median PFS vs temsirolimus (15.5 vs 6.2 months; p < 0.0001). Median OS was not reached for ibrutinib vs 21.3 months for temsirolimus (HR, 0.76 [95% CI, 0.53-1.09]; p = 0.1324). The difference was not statistically significant; however, it should be noted that 32 (23%) of temsirolimus patients (23%) crossed over to ibrutinib. 1-year survival rates were 68% for ibrutinib and 61% for temsirolimus. After a median follow up of over 3 years, median OS was nearly 7 months longer with ibrutinib vs temsirolimus (30.3 vs 23.5 months; HR = 0.74 [0.54-1.02]; p = 0.0621). Further in a pooled analysis 3.5 year follow up across studies 1104, SPARKLE and RAY, Janssen submitted that Rule *et al* (2019) demonstrated overall, median PFS and OS were 12.5 (95%CI: 9.8-16.6) and 26.7 (95%CI: 22.5-38.4) months, respectively. Patients receiving ibrutinib in second line had better outcomes than those treated in later lines (>1 prior line): median PFS and OS were 25.4 months (95%CI: 17.5- 57.5) and not reached [NR; 95%CI: 36.0-not estimable)], respectively.

For treatment of adults with Waldenström's in one prior therapy or first line treatment for patients unsuitable for chemo-immunotherapy, Janssen submitted that study NCT01614821 was a prospective open-label, multicentre, single-arm phase 2 study (n=63) where the primary endpoint was the rate of overall response and secondary endpoints included survival efficacy outcomes such as PFS, OS and safety. At 24 months, the estimated rate of PFS was 69.1% (95% CI, 53.2-80.5) and the estimated rate of OS was 95.2% (95% CI, 86.0-98.4). Ibrutinib had an overall response of 91% which had demonstrated single active agent for relapsed or refractory Waldenström's macroglobulinaemia (WM) where European Medicines Agency (EMA) approval was attained. Janssen further submitted that iNNOVATE was an ongoing, randomised phase III, placebo-controlled study where a subset analysis was performed from the non-randomised, single-arm group of patient's refractory to rituximab who were treated with ibrutinib (n=31). At a median follow-up of 18·1 months (17·5 – 18·9), the proportion of patients with an overall response was 28 [90%] of 31 (22 [71%] of patients had a major response), the estimated 18-month PFS rate was 86% (95% CI 66–94), and the estimated 18 month OS rate was 97% (95% CI 79–100). This study population differed in a clinically significant way from NCT01614821 with respect to higher median lines of previous regimens and its focus on patient's refractory to the most recent rituximab containing regiment.

With respect to the procedural handling of this complaint, Janssen noted that the exact words of the complainant were, 'There is no OS benefit with the drug'. Janssen submitted that this was mentioned three times in the complaint and was in itself an all-embracing complaint, which was misleading, not capable of substantiation and factually incorrect. Janssen submitted that it had demonstrated and documented survival data for its licensed indications with data described above and within Section 5.1 of the Imbruvica SPC.

Janssen noted that Paragraph 2.2 of the Constitution and Procedure stated 'Rulings are made on the basis that a complainant has the burden of proving their complaint on the balance of probabilities'. Janssen submitted that the complainant had not achieved this as he/she alleged no survival data across Imbruvica's indications when survival data had been demonstrated across its indications as noted above and within the SPC.

**PANEL RULING**

The Panel noted Janssen's submission that 'Destination survival' was a strapline that accompanied the Imbruvica logo. The Panel considered that this strapline was a claim for Imbruvica. Clause 7.2 required claims to be, *inter alia*, accurate, balanced, fair, objective and unambiguous. Clause 7.4 stated that claims must be capable of substantiation.

The Panel noted that the 'Getting started' leaflet contained Imbruvica's logo with the strapline 'Destination survival' on multiple pages alongside images depicting space travel. The leaflet was entitled, 'Getting started with once-daily, oral, single-agent Imbruvica (ibrutinib)'. The second page of the leaflet listed all of Imbruvica's indications. The third and fourth pages of the leaflet referred to both CLL and MCL [mantle cell lymphoma] dosage instructions. In the Panel's view, the leaflet was not solely about CLL and therefore the strapline 'Destination survival' might be considered in the context of all Imbruvica's indications.

The Panel considered that health professionals working in oncology would, on the balance of probabilities, associate the strapline 'Destination survival' with overall survival benefit.

The Panel noted Janssen's submission that data supporting ibrutinib's efficacy in improving overall survival in CLL for both patients with untreated CLL as well as patients who had received at least one prior therapy was included in Section 5.1 of the SPC and published by Burger *et al* (2015) and Byrd *et al* (2014), respectively.

The Panel noted that Burger *et al* (2015) was a Phase III trial comparing ibrutinib with chlorambucil in previously untreated CLL. The Panel noted that the study authors stated that ibrutinib resulted in significantly longer progression-free survival (primary endpoint) and significantly prolonged overall survival (secondary endpoint) vs chlorambucil.

The Panel noted that Byrd *et al* (2014) was a Phase III trial comparing ibrutinib with ofatumumab in previously treated CLL. The Panel noted that the study authors stated that ibrutinib significantly improved progression-free survival (primary endpoint) and significantly improved overall survival (secondary endpoint) vs ofatumumab.

The Panel considered the body of clinical data provided by Janssen. The Panel noted that not all studies across all Imbruvica's licensed indications had demonstrated a statistically significant overall survival benefit vs the comparator arm. For example, in the HELIOS study (Chanan-Khan *et al*, 2016), which was a Phase III trial of ibrutinib combined with bendamustine and rituximab compared with placebo (plus bendamustine and rituximab) in previously treated CLL, the authors stated that there was no statistically significant difference in overall survival between the treatment arms. The Panel further noted Janssen's submission that the difference in overall survival between treatment arms in a mantle cell lymphoma study (MCL3001) of ibrutinib vs temsirolimus was not statistically significant. Furthermore, the Panel noted that for the Waldenström's macroglobulinaemia indication, the efficacy of ibrutinib was evaluated in an open-label, single-arm Phase II trial (NCT01614821) and in a non-randomised, single-arm subset analysis of an ongoing Phase III trial (iNNOVATE study).

The Panel noted its comments above. Based on the information before it, the Panel considered that not all of Imbruvica's licensed indications had the body of evidence to support the claim 'Destination survival' which appeared as part of the Imbruvica logo and was included in the leaflet in question which featured all of Imbruvica's indications. The Panel considered, therefore, that the claim was misleading and incapable of substantiation and a breach of Clauses 7.2 and 7.4 was ruled.

The Panel considered that Janssen had failed to maintain high standards in this regard and a breach of Clause 9.1 was ruled.

The Panel noted the complainant's allegation that the term 'Destination survival' in the 'Getting started' leaflet was misleading in the absence of any survival data within the leaflet. The Panel noted Janssen's submission that the leaflet was intended as a user-friendly simplification of the prescribing information and contained no efficacy data. The Panel did not consider that the claim in question was misleading by virtue of the leaflet not containing survival data as alleged and, in that regard, ruled no breach of Clause 7.2.

**Complaint received** **2 December 2018**

**Case completed** **12 July 2019**

**CASE AUTH/3130/12/18**

# ANONYMOUS v GLAXOSMITHKLINE

## Arrangements for a meeting and alleged use of LinkedIn to promote a medicine

**An anonymous contactable individual complained about a poster inviting pharmacists to attend a continuing professional development (CPD) meeting to look at asthma medication reviews and a minor illness referral service. The name of a retail pharmacy group appeared at the top of the poster and the GlaxoSmithKline logo appeared at the bottom. The complainant also drew attention to a LinkedIn post about Bexsero (meningococcal group B vaccine) from several employees of GlaxoSmithKline.**

**The detailed response from GlaxoSmithKline is given below.**

**The complainant alleged that a poster for the CPD meeting had been circulated by GlaxoSmithKline and it was not clear if the meeting would be sponsored by the company or if its medicines would be promoted. If a promotional meeting was to be held under the guise of a CPD meeting, then the complainant considered that GlaxoSmithKline was pulling the wool over health professionals' eyes. As the poster stated that the meeting would start at 7pm at a restaurant and a three-course meal would be provided, the complainant was concerned that the hospitality was the main reason and attraction to the event. The complainant noted that there was no date as to when the poster had been produced; he/she was shocked that it was shared actively on Facebook and had no means of being directed to relevant personnel.**

**The Panel noted GlaxoSmithKline's detailed submission about communications between the retail pharmacy group and GlaxoSmithKline's representatives, and between the GlaxoSmithKline representatives and GlaxoSmithKline management.**

**The Panel noted GlaxoSmithKline's submission that it was first approached in November 2018 with regard to sponsoring the meeting and that on 26 November it became aware that the invitation, with the company's logo, had been advertised the previous day by the retail pharmacy group before sponsorship of the meeting had been confirmed and without GlaxoSmithKline's approval or knowledge.**

**It appeared to the Panel from the emails provided that GlaxoSmithKline made a final maximum sponsorship offer on 9 December which was confirmed by the retail pharmacy group.**

**The Panel noted that GlaxoSmithKline was informed of the complaint on 7 December and a GlaxoSmithKline representative emailed the retail pharmacy group on 12 December, the day of the meeting, to withdraw GlaxoSmithKline's offer of sponsorship. The Panel noted GlaxoSmithKline's submission that the retail pharmacy group had evidently continued to circulate the invitation clearly ignoring its representative's warning that the invitation was not compliant, and that sponsorship still needed to be agreed and confirmed. The Panel noted GlaxoSmithKline's submission that following this exchange, it did not sponsor or attend the meeting and had no further involvement.**

**The Panel noted that it was not clear how and when the complainant had seen the invitation. The complaint was received by the PMCPA on 3 December and referred to the invitation at issue being circulated by GlaxoSmithKline and actively shared on Facebook. GlaxoSmithKline had submitted that it did not circulate the invitation at issue. The Panel noted that it appeared, according to the information before it, that the retail pharmacy group advertised the invitation on 25 November. The local pharmaceutical committee (LPC) also wanted to send out an invitation around 5 December but it was not clear if it did.**

**The Panel noted the complainant had the burden of proving his/her complaint on the balance of probabilities and in the Panel's view it appeared that GlaxoSmithKline had not confirmed sponsorship of the meeting when the retail pharmacy group advertised the meeting with an invitation which contained the company's logo on 25 November, nor had sponsorship been confirmed prior to 3 December when the complaint was received. Therefore, the Panel considered that, when the complainant received the invitation, GlaxoSmithKline was not responsible for sponsorship of the meeting and so it did not need to declare sponsorship. No breach was ruled in that regard.**

**Given this ruling, the invitation was not disguised promotion, nor was GlaxoSmithKline responsible for the offer of a three course meal. The Panel therefore ruled no breaches of the Code including Clause 2.**

**The complainant provided a copy of a LinkedIn post which consisted of a photograph of what was assumed to be a GlaxoSmithKline office above which was stated 'Looks like another potential vaccines blockbuster!'. Below the photograph was the statement 'GlaxoSmithKline weighs men B shot Bexsero's promise against gonorrhea' followed by the pharmaceutical industry news agency website (fiercepharma.com).**

**The complainant alleged that the LinkedIn post 'by several members of GSK' promoted its medicine directly to the public as LinkedIn was a very public platform.**

**The Panel noted that LinkedIn was different to some other social media platforms in that it was a business and employment-orientated network and**

**was primarily, although not exclusively, associated with an individual's professional heritage and current employment and interests. In the pharmaceutical industry, the Panel noted that an individual's network might, albeit not exclusively, be directly or indirectly associated with the healthcare industry. In the Panel's view, it was of course not unacceptable for company employees to use personal LinkedIn accounts and whether the Code applied would be determined on a case-by-case basis taking into account all the circumstances including: the content, any direct or indirect reference to a product, how the information was disseminated on LinkedIn, the company's role in relation to the availability of the content and whether such activity was instructed or encouraged by the company. If activity was found to be within the scope of the Code, the company would be held responsible.**

**The Panel noted that the post provided by the complainant was titled 'Looks like another potential vaccines blockbuster!' which appeared in a different font to the rest of the post and was not stated in the linked article. It was not entirely clear to the Panel if this text was added when the post was shared or if it was part of the original post. GlaxoSmithKline made no submission in this regard. This was followed by a picture of a building below which was the statement 'GlaxoSmithKline weighs men B shot Bexsero's promise against gonorrhoea' followed by fiercepharma.com. The Panel noted the complainant's concern that a prescription only medicine was being promoted to the public. The Panel noted that Bexsero was indicated for active immunisation of individuals from 2 months of age and older against invasive meningococcal disease caused by Neisseria meningitidis group B.**

**The Panel noted that the full article which could be accessed through the fiercepharma.com link within the post explained that a study showed that meningitis B vaccines like GlaxoSmithKline's Bexsero could provide some protection against gonorrhea and the company was analysing whether to move forward with testing in the disease area. It further stated that GlaxoSmithKline could not comment further as work remained exploratory and that the company had not yet started any tests in the disease area.**

**The Panel noted GlaxoSmithKline's submissions that the article in question had never been posted or shared on any of its corporate external-facing channels and that the LinkedIn post in question was shared on LinkedIn by a contractor of GlaxoSmithKline Global (not GlaxoSmithKline UK Pharma), on their personal LinkedIn account. The Panel noted, however, that the GlaxoSmithKline global headquarters were based in the UK and the contractor who shared the post was based in the UK.**

**The Panel noted GlaxoSmithKline's submission that it played no role in the availability of the content of the post, nor did it instruct or encourage the contractor to disseminate it. According to GlaxoSmithKline, its policies and training made it clear to employees and contractors that content posted and shared on personal social media accounts risked being perceived as company-endorsed communication, and as such employees and contractors should never post or share content that mentioned or referred to prescription medicines other than content that had been specifically approved by GlaxoSmithKline for the general public audience; the contractor in question was trained on the global social media policy and had acted in breach of it.**

**Contrary to GlaxoSmithKline's submission the Panel did not consider that the issues raised by the complainant required GlaxoSmithKline to train all staff in depth on its product portfolio, but in the Panel's view it was reasonable for it to train all staff on its social media policy which according to GlaxoSmithKline had been done.**

**In the Panel's view, activity conducted on social media that could potentially alert one's connections to the activity might be considered proactive dissemination of material. In addition, an individual's activity and associated content might appear in that individual's list of activities on his/her LinkedIn profile page which was visible to his/her connections; an individual's profile page was also potentially visible to others outside his/her network depending on the individual's security settings.**

**The Panel noted that the post itself was headed 'Looks like another potential vaccines blockbuster' and referred to Bexsero as a 'men B shot' and its 'promise against gonorrhea' which was an unlicensed indication. The Panel noted that Bexsero was available as a prescription only medicine in the UK. The Panel further noted that the linked article referred to a study and stated, *inter alia*, 'meningitis B vaccines like GlaxoSmithKline's Bexsero can provide some protection against gonorrhoea ...'.**

**The Panel did not know how many connections the named contractor had on LinkedIn and if they were all health professionals; the company made no submission in that regard. However, as it was a personal LinkedIn account, the Panel considered that, on the balance of probabilities, not all the contractor's connections would have been health professionals and, therefore, sharing the LinkedIn post and associated article with his/her network constituted promotion of a prescription-only medicine to the public and might encourage members of the public to ask their health professional to prescribe Bexsero. Breaches of the Code were ruled including that high standards had not been maintained.**

**The contractor had acted in breach of company policy and training. The Panel considered that the particular circumstances of this case did not warrant a ruling of a breach of Clause 2 of the Code which was a sign of particular censure and reserved for such use.**

An anonymous contactable individual complained about a poster inviting pharmacists to attend a continuing professional development (CPD) meeting taking place on 12 December 2018 which would look at asthma medication reviews and a minor illness referral service. The name of a retail pharmacy group appeared at the top of the poster and the

GlaxoSmithKline logo appeared at the bottom. The complainant also drew attention to a LinkedIn post about Bexsero (meningococcal group B vaccine) from individuals at GlaxoSmithKline.

**1 CPD Meeting**

**COMPLAINT**

The complainant provided a copy of a meeting poster which he/she alleged had been circulated by GlaxoSmithKline.

The complainant stated that he/she was aware of the ABPI requirements and that from the outset it was not clear if the meeting would be sponsored by GlaxoSmithKline and, without an agenda, it was not clear if the company's medicines would be promoted. If a promotional meeting was to be held under the guise of a CPD meeting, then the complainant considered that GlaxoSmithKline was pulling the wool over health professionals' eyes. The poster stated that the meeting would start at 7pm at a restaurant and a three-course meal would be provided. Given this statement, the complainant was concerned that the hospitality was the main reason and attraction to the event. The complainant noted that there was no date as to when this poster had been produced. The complainant stated that he/she was shocked that the poster was shared actively on Facebook and had no means of being directed to relevant personnel.

When writing to GlaxoSmithKline, the Authority asked it to consider the requirements of Clauses 9.10, 12.1, 22.1, 22.2, 22.4, 9.1 and 2.

**RESPONSE**

GlaxoSmithKline submitted that the poster was an invitation created and circulated by the named retail pharmacy group without the company's prior knowledge or approval and before sponsorship of the meeting had been agreed.

GlaxoSmithKline explained that the retail pharmacy group owned and operated a chain of pharmacies across a named geography. Staff at the retail pharmacy group first approached a GlaxoSmithKline representative on 20 November 2018 to ask whether the company would be interested in sponsoring the meeting in question. In accordance with GlaxoSmithKline's standard procedure the representative requested further details about the agenda, venue, attendees and speakers to assess whether the meeting would comply with the Code for sponsorship purposes. It was made clear that GlaxoSmithKline followed a strict approval process for sponsorship of meetings.

The retail pharmacy group provided an agenda for the meeting and a sponsorship proposal for consideration by GlaxoSmithKline on 22 November. The meeting would be held at a local restaurant and would provide two training sessions to pharmacists on (i) Medicines Use Reviews for asthma medicines and (ii) treating low acuity minor illness from the pharmacy. The retail pharmacy group requested sponsorship for catering at a given cost per head for a maximum of 70 attendees and in return offered promotional stand space; pharmacists would have time before the training to speak to GlaxoSmithKline representatives. As was standard procedure for sponsorship of third party meetings, GlaxoSmithKline would have no input into the agenda, organisation or administration of the meeting other than to ensure compliance with the Code.

On 23 November, the first representative introduced his/her contact at the retail pharmacy group to a second representative who would be responsible for any sponsorship arrangement and the approval process going forward. The retail pharmacy group replied that it would send the proposal form over outlining the details of the proposed meeting.

However, on 26 November, the retail pharmacy group emailed an invitation for the meeting and implied that it had already been circulated with 30 confirmed attendees. GlaxoSmithKline had not previously seen a copy of the invitation and had not been given any indication that the retail pharmacy group intended to circulate an invitation for the meeting displaying the company's logo. GlaxoSmithKline submitted that at this stage its due diligence processes were still ongoing and it had not confirmed that it would sponsor the meeting and had not entered into a contract with the retail pharmacy group.

On receipt of the email of 26 November attaching the invitation, the second representative immediately sent details of the meeting, sponsorship proposal and invitation to his/her first line manager for discussion in accordance with company procedures for sponsored meetings and immediately replied to the retail pharmacy group to make clear that sponsorship for the meeting still had to be authorized and confirmed.

After promptly reviewing the materials, the first line manager's feedback included that the invitation needed more than just the GlaxoSmithKline logo on it and he/she asked the second representative to send the amended invitation from the retail pharmacy group and stated that the sponsorship requested exceeded the lower amount usually paid by GlaxoSmithKline for a stand at sponsored events of that size.

The first line manager also referred the second representative to guidance on GlaxoSmithKline's internal field portal.

In accordance with his/her manager's instructions, the second representative informed the retail pharmacy group on 27 November that the invitation needed to be amended to comply with industry standards. On 28 November, the representative further confirmed that he/she would inform the pharmacy group if the sponsorship was approved by management and (if confirmed) amend the invitation.

During the week commencing 3 December the second representative and the retail pharmacy group discussed progress on GlaxoSmithKline's internal

assessment of the sponsorship proposal and a number of emails were exchanged to finalise the maximum amount of sponsorship GlaxoSmithKline could offer. A final maximum offer of lower than that requested was made by GlaxoSmithKline on 9 December, however, this was still subject to management authorization. Having confirmed the sponsorship amount, the second representative would have continued to follow company process for approval of sponsored meetings as outlined below.

Once informed of the complaint on 7 December the second representative emailed the retail pharmacy group on 12 December to withdraw GlaxoSmithKline's offer of sponsorship as the retail pharmacy group had evidently continued to circulate the invitation, clearly ignoring the representative's warning that the invitation was not compliant, and that sponsorship still needed to be agreed and confirmed. The representative further asked the pharmacy group to remove GlaxoSmithKline's logo from any further communications about the meeting. The pharmacy group replied claiming that it had not been told that use of the GlaxoSmithKline logo was unauthorized and that the company had been advised that the invitation had already been sent out on the 26 November. However, it was quite clear that GlaxoSmithKline did inform the retail pharmacy group on 27 November that the invitation was not compliant with industry standards and would need to be amended.

GlaxoSmithKline stated that following this exchange, it did not sponsor or attend the meeting. The company confirmed that it had not had any further involvement in or further correspondence with the pharmacy group after this exchange about the meeting.

GlaxoSmithKline recognised that the invitation did not comply with the Code as it included the company's logo without clearly declaring the company's sponsorship of the meeting and role in the event. However, GlaxoSmithKline asserted that it had not created the invitation which was circulated without prior notice and approval from the company, and before the company had confirmed to the retail pharmacy group that it was authorized to sponsor the meeting.

GlaxoSmithKline stated that it had procedures in place to ensure that items relating to meetings it sponsored included a declaration of the company's sponsorship and description of the company's role in the event.

GlaxoSmithKline explained that training on sponsored meetings was provided to all field force and first line sales managers, and the training slides were accessible to all representatives. The slides set out the process for approval of sponsored third-party meetings and guidance to ensure compliance with applicable Code provisions, including steps to ensure that meetings had a clear educational content, were for the benefit of patients, the sponsorship costs were in line with fair market value and the venues were appropriate. The training also made it clear that GlaxoSmithKline's sponsorship must be declared on the agenda and all papers relating to the meeting in order to comply with the Code. Examples of appropriate declarations provided in the slides included: 'GSK have sponsored the catering for this event' and 'GSK have sponsored this meeting through the purchase of stand space'.

GlaxoSmithKline stated that as evidenced in email exchanges provided, the invitation was promptly reviewed by the relevant first line sales manager and the absence of required information was flagged in accordance with company procedure; the retail pharmacy group was clearly informed that the invitation did not comply with industry standards and needed to be amended.

As the second representative had discussed in principle the sponsorship details with his/her first line sales manager and assessed fair market value of the sponsorship offer, the next stage in GlaxoSmithKline's sponsored meeting process would have been for the representative to review the agenda and all materials related to the meeting to ensure compliance with the Code. An engagement form would then be completed by the representative, including details of the sponsorship, and submitted for manager approval. A contract would then have been generated on the basis of GlaxoSmithKline's template for sponsored meetings. This template contract included provisions which required the event organiser to 'ensure that all potential attendees are aware, before the date of the Meeting, that GSK is providing Sponsorship for the Meeting and, if relevant, whether GSK staff are attending and whether GSK will have a promotional stand at the Meeting'. Further, the contract required that all materials produced by the organiser relating to the meeting included the following declarations 'in a sufficiently prominent position to ensure that those reading or viewing the materials are aware of the Sponsorship and any GSK presence at the outset'.

a) 'GlaxoSmithKline has provided Sponsorship towards the [stand space, venue, equipment, catering and / or speaker] costs of this meeting but have had no input into or influence over the agenda or content or selection of speakers.'

b) 'GlaxoSmithKline shall have [a stand at the Meeting promoting GlaxoSmithKline products and] staff will be present at the meeting.'

Further, the agreement prohibited the organiser from using GlaxoSmithKline's logo on any written materials without its consent. However, as the sponsorship did not proceed past the due diligence stage of the company's process, a contract was not generated for the meeting.

GlaxoSmithKline noted that the retail pharmacy group had circulated an invitation without the necessary declarations of sponsorship. GlaxoSmithKline did not approve, disseminate or know about the invitation. When the invitation was circulated, GlaxoSmithKline had not confirmed that it would sponsor the meeting, the sponsorship proposal was still going through its approval process, and the retail pharmacy group was fully aware of that. Had the sponsorship been agreed, any papers relating to the meeting would have gone

through GlaxoSmithKline's approval process to ensure compliance with the Code. GlaxoSmithKline thus denied any breach of Clauses 9.10 and 22.4.

GlaxoSmithKline recognised that the invitation did not comply with Clause 12.1 as it did not clearly declare that the company (and other sponsors) would have a promotional stand at the meeting staffed by representatives. However, the invitation was circulated before GlaxoSmithKline's knowledge and approval and before it finally confirmed that it would sponsor the meeting.

As explained above, GlaxoSmithKline had procedures and template contracts in place to ensure that where GlaxoSmithKline had purchased stand space at a third party organised event, a declaration was made to that effect on all papers about the meeting. The relevant GlaxoSmithKline personnel took all appropriate steps to comply with these procedures. The company denied any breach of Clause 12.1.

GlaxoSmithKline acknowledged that the reference to a three-course meal on the invitation might appear to be the main attraction to the event and would not have been appropriate or proportionate to the meeting. However, GlaxoSmithKline only knew that the meal would be provided when it received the invitation on 26 November. GlaxoSmithKline was also not informed that the meal would expressly be promoted or highlighted in any meeting materials.

GlaxoSmithKline repeated that it had procedures in place to ensure that sponsored meetings were held at appropriate venues conducive to the main purpose of the meeting and that any subsistence provided was appropriate and secondary to the nature of the meeting. Further, GlaxoSmithKline's template contract for sponsored meetings required the organiser of the meeting to comply with the principles set out in Clause 22.

GlaxoSmithKline reiterated that it did not sponsor this meeting. However, had sponsorship been agreed, any hospitality related to the meeting would have gone through due process to ensure compliance with the Code. GlaxoSmithKline denied any breach of Clauses 22.1 and 22.2.

GlaxoSmithKline stated that it tried to maintain high standards at all times and had appropriate policies and procedures in place to ensure compliance with the Code as evidenced above.

GlaxoSmithKline reiterated that it did not create, approve or circulate the invitation. The invitation was created and circulated by the retail pharmacy group without the company's prior knowledge or approval and before sponsorship arrangements for the meeting had been agreed.

GlaxoSmithKline submitted that it had promptly informed the pharmacy group of the non-compliance and had the sponsorship been agreed, the company would have ensured that all materials about the event complied with the Code in accordance with its standard procedures.

On receiving the complaint and thus knowing that the retail pharmacy group had apparently continued to circulate what it knew was a non-compliant invitation for the meeting, GlaxoSmithKline promptly withdrew its sponsorship offer and asked for its logo to be removed from all future communications related to the meeting.

GlaxoSmithKline asserted that it did not create nor distribute any materials that discredited or reduced confidence in the industry, and it took appropriate action to rectify the actions of the retail pharmacy group to maintain high standards. GlaxoSmithKline denied any breach of Clause 9.1 or 2.

**PANEL RULING**

The Panel noted GlaxoSmithKline's detailed submission about communications between the lead pharmacist at the retail pharmacy group and its sales representatives, and between the sales representatives and management. The Panel also noted the timeline of events as revealed by the emails between the parties. The Panel noted that the retail pharmacy group had communications with three separate representatives about sponsorship arrangements.

The Panel noted GlaxoSmithKline's submission that it was first approached on 20 November 2018 with regard to sponsoring the meeting. The Panel noted that on 26 November GlaxoSmithKline became aware that the invitation at issue, which contained the company's logo, had been advertised the previous day by the retail pharmacy group without GlaxoSmithKline's approval or knowledge. The Panel noted GlaxoSmithKline's submission that this was before sponsorship of the meeting had been confirmed with the retail pharmacy group. The Panel noted that following this GlaxoSmithKline remained in discussion with the retail pharmacy group with regard to its potential sponsorship of the meeting.

It appeared to the Panel from the emails provided that GlaxoSmithKline made a final maximum sponsorship offer on 9 December which was confirmed the same day by the retail pharmacy group.

The Panel noted that when GlaxoSmithKline was informed of the present complaint on 7 December, a GlaxoSmithKline representative emailed the retail pharmacy group on 12 December, the day of the meeting, to withdraw GlaxoSmithKline's offer of sponsorship. The Panel noted GlaxoSmithKline's submission that the retail pharmacy group had evidently continued to circulate the invitation at issue, clearly ignoring its representative's warning that the invitation was not compliant, and that sponsorship still needed to be agreed and confirmed. The Panel noted GlaxoSmithKline's submission that following this exchange, it did not sponsor or attend the meeting and had no further involvement in or further correspondence with the retail pharmacy group.

The Panel noted that it was not clear how and when the complainant had seen the invitation

at issue. The Panel noted that the complaint was received by the PMCPA on 3 December and referred to the invitation at issue being circulated by GlaxoSmithKline and actively shared on Facebook. The Panel noted GlaxoSmithKline's submission that it did not circulate the invitation at issue. The Panel noted that according to the information before the Panel, it appeared that the retail pharmacy group advertised the invitation on 25 November. The local pharmaceutical committee (LPC) also wanted to send out an invitation around 5 December but it was not clear if it did.

The Panel noted that Clause 9.10 stated that material relating to medicines and their uses, whether promotional or not, and information relating to human health or diseases which was sponsored by a pharmaceutical company must clearly indicate that it had been sponsored by that company. The Panel did not consider that Clause 9.10 was relevant to the meeting invitation at issue and made no ruling in this regard.

The Panel noted that Clause 22.4 stated that when meetings were sponsored by pharmaceutical companies, that fact must be disclosed in all of the papers related to the meetings and in any published proceedings. The declaration of sponsorship must be sufficiently prominent to ensure that readers were aware of it at the outset.

The Panel noted GlaxoSmithKline's submission that at the time the meeting invitation was circulated it had not confirmed that it would sponsor the meeting. The complainant had the burden of proving his/her complaint on the balance of probabilities and in the Panel's view it appeared that GlaxoSmithKline had not confirmed sponsorship of the meeting when the retail pharmacy group advertised the meeting with an invitation which contained the company's logo on 25 November, nor had sponsorship been confirmed prior to 3 December when the complaint was received. Therefore, the Panel considered that, when the complainant received the invitation, GlaxoSmithKline was not responsible for sponsorship of the meeting and it ruled no breach of Clause 22.4.

The Panel noted the complainant's concern that it was not clear from the invitation at issue if GlaxoSmithKline's medicines were to be promoted and if a promotional meeting was to be held under the guise of a CPD meeting, GlaxoSmithKline was pulling the wool over health professionals' eyes. Clause 12.1 stated that promotional material and activities must not be disguised. The Panel noted its comments above with regard to GlaxoSmithKline not being responsible for the sponsorship of the meeting when it was advertised on the 25 November or prior to 3 December when the complaint was received as it had not yet confirmed sponsorship of the meeting and the Panel therefore ruled no breach of Clause 12.1. The Panel noted the complainant's concern that the offer of a three-course meal on the invitation was the main reason and attraction to the event. The Panel noted that Clause 22.1 stated, *inter alia*, that hospitality must be strictly limited to the main purpose of the event and must be secondary to the purpose of the meeting ie subsistence only. The level of subsistence offered must be appropriate and not out of proportion to the occasion.

The Panel noted GlaxoSmithKline's submission that reference to a three-course meal on the invitation might appear to be the main attraction to the event and would not have been appropriate or proportionate to the meeting. The Panel noted GlaxoSmithKline's submission that it only became aware that a three-course meal would be provided when it received the invitation on 26 November. The Panel noted its comments above with regard to GlaxoSmithKline not being responsible for the invitation when it was advertised on the 25 November or prior to 3 December when the complaint was received, and the Panel therefore ruled no breach of Clause 22.1.

The Panel noted that Clause 22.2 stated that the cost of a meal (including drinks) provided by way of subsistence must not exceed £75 per person, excluding VAT and gratuities. The Panel, however, did not consider that there was an allegation with regards to the cost of the meal and therefore made no ruling.

The Panel noted its comments and rulings of no breach of the Code above and therefore ruled no breach of Clauses 9.1 and 2.

**2 LinkedIn posting**

The complainant provided a copy of a LinkedIn post which consisted of a photograph of what was assumed to be a GlaxoSmithKline office block above which was stated 'Looks like another potential vaccines blockbuster!'. Below the photograph was the statement 'GlaxoSmithKline weighs men B shot Bexsero's promise against gonorrhea' followed by a pharmaceutical industry news agency website address.

**COMPLAINT**

The complainant alleged that the LinkedIn post 'by several members of GSK' promoted its medicine directly to the public as LinkedIn was a very public platform.

When writing to GlaxoSmithKline, the Authority asked it to consider the requirements of Clauses 11.1, 26.1, 26.2, 9.1 and 2.

**RESPONSE**

GlaxoSmithKline submitted that the article in question had never been posted or shared on a GlaxoSmithKline corporate social media account. GlaxoSmithKline provided a copy of its standard operating procedure (SOP) for external and internal communications activities on behalf of the company. The SOP included a section on 'Expressions of personal opinion to a public audience, including personal use of social media'. The SOP highlighted that 'Personal use of social media can be perceived

as company-endorsed communication' and 'posts on their social media networks, can be visible to a wide range of audiences, including colleagues, patients, healthcare professionals …'. The SOP further stated that 'GSK Staff must not publicly express opinions about prescription products – whether GSK products or competitor products'.

In addition to the SOP, mandatory training was provided to all staff on the use of social media (training slides were provided). The training reinforced the far-reaching impact of sharing content on social media and possible risks for the company, and stated that GlaxoSmithKline staff should 'not create posts, make comments or share content that could be perceived as promoting our pharmaceutical products' or 'respond to third-party social media posts which mention GSK brands or competitor brands'. The training further stated that 'In general, if approved content appears on a GSK external channel used for our general public audience (GSK Facebook, YouTube, GSK LinkedIn or GSK Twitter), you can share it'.

GlaxoSmithKline stated that it never shared the article on any of its corporate external-facing channels (including GlaxoSmithKline Facebook, YouTube, GlaxoSmithKline LinkedIn or GlaxoSmithKline Twitter) and that it had appropriate SOPs and training in place to ensure compliance with Clauses 11.1, 26.1 and 26.2 and to ensure that high standards were maintained and that staff did not distribute any materials on social media that might discredit or reduce confidence in the industry.

A significant number of employees had personal social media accounts. Bearing in mind the special nature of medicines and the requirements under the Code, GlaxoSmithKline conducted a robust and thorough internal investigation and discovered that the LinkedIn post linking to the article published by the pharmaceutical industry news agency was shared on LinkedIn by an employee of GlaxoSmithKline Global (not GlaxoSmithKline UK Pharma), on their personal LinkedIn account. This was in direct contravention of the GlaxoSmithKline SOP for external and internal communications activities on behalf of GlaxoSmithKline as well as the mandatory training. As such, the matter was being dealt with directly with the individual concerned.

GlaxoSmithKline stated that it took its responsibility very seriously for ensuring all employees globally knew of, and truly understood, its policy on the personal use of social media. That was why relevant training was delivered as part of GlaxoSmithKline's global mandatory training to all employees entitled 'Living our Values and Expectations'. In addition, there were plans for GlaxoSmithKline's global communications team to run an employee advocacy programme in 2019 to help further explain the policy by sharing examples of acceptable use. Further to this, the company would reinforce to all employees the social media policy and, in addition, external communications, compliance and legal teams would ensure that GlaxoSmithKline policies adequately addressed the rapidly progressing area of social media.

GlaxoSmithKline did not believe that it had failed to maintain high standards or had brought the industry into disrepute. The company played no role in the availability of the content of the post, nor did it instruct or encourage the employee to disseminate it. GlaxoSmithKline's policies and training made it quite clear to all employees that content posted and shared on personal social media accounts risked being perceived as company-endorsed communication, and as such employees should never post nor share any content that mentioned or referred to prescription medicines (whether GlaxoSmithKline or competitor products) other than content that had been specifically approved by GlaxoSmithKline for the general public audience.

GlaxoSmithKline submitted that it had continued to work hard to develop comprehensive and clear guidelines for its employees in the rapidly changing area of social media, whilst maintaining an appropriate and realistic balance between the rights of its employees as individuals and their responsibilities as GlaxoSmithKline employees.

GlaxoSmithKline denied any breach of Clauses, 11.1, 26.1, 26.2, 9.1 and 2 of the Code.

In response to a request for further information, GlaxoSmithKline noted that the article associated with the LinkedIn post stated that the company was assessing the potential for further investigation of Bexsero in preventing gonorrhoea. GlaxoSmithKline stated that it had not issued any press release or proactively sought to engage with the media other than to provide reactive statements, in either the UK or the US, about its intention to explore the use of Bexsero to prevent gonorrhoea. The article was written and published by an independent US pharmaceutical industry news agency. Before publishing the article, the agency contacted the US communications team at GlaxoSmithKline, unsolicited, to ask whether efforts were under way to develop a new gonorrhoea vaccine following recent reports. In response, the company provided a generic statement to clarify that it was, at the time, talking to health authorities and external researchers to determine the potential for further investigation, that any efforts in the area remained exploratory, and that no decision had yet been taken as to whether to conduct and fund company-sponsored studies for Bexsero or any other vaccine in this area. The article also quoted from a second article written and published independently by another third party, and to which GlaxoSmithKline had again only provided reactive statements to specific questions posed by a journalist. The article was clearly intended for a US audience; it focussed on the prevalence of gonorrhea in the US and the success of Shingrix in the US, a GlaxoSmithKline medicine licensed but not available in the UK. It would therefore be obvious to readers that the article did not concern the UK product market.

The individual who shared the article on LinkedIn was a contract worker engaged by GlaxoSmithKline for a role based at the company's headquarters in the UK. The employee had LinkedIn followers

based in the UK, however he/she also had a number of followers based abroad including the US. The employee in question had been engaged by GlaxoSmithKline for a couple of years.

GlaxoSmithKline noted that the individual in question did not work in a promotional role and his/her role was never customer facing. The company provided appropriate training tailored to the roles of its employees and contract workers and it confirmed that the contractor had completed the global mandatory social media training referred to above, before the date of the complaint. GlaxoSmithKline reiterated that the contractor had acted in breach of company policy and training requirements, and the matter had been dealt with directly.

GlaxoSmithKline explained that it employed a significant number of employees and contractors in non-commercial, non-promotional roles that were based in the UK, including in manufacturing, supply chain, R&D and head office based roles such as HR and recruitment, finance, regulatory and legal. It was therefore unreasonable and unrealistic to expect companies like GlaxoSmithKline, with multiple operations in the UK, to provide in depth training to all of its employees and contractors in the UK on the company's entire product portfolio, the significance of licensed/unlicensed products and indications, prescription and non-prescription, the significance of different clinical trial phases, and so on, to enable them to distinguish between material that would be considered promotional or not, where this was not relevant to their roles.

As noted above, GlaxoSmithKline had training and policies in place to ensure that all employees and contractors globally were aware of the risks of posting material on their personal social media accounts that might be perceived as promotional. GlaxoSmithKline did not proactively engage with the pharmaceutical industry news agency to publish the article, nor did it instruct or encourage the contractor to share the article on LinkedIn. GlaxoSmithKline stated that it regretted that a company-affiliated individual shared an article mentioning GlaxoSmithKline branded prescription products on a public social media page, however the company had taken all reasonable steps to train employees on this matter in order for this not to happen. The article was not shared with any promotional intent and it would have been obvious to any reader that the article was intended for a US audience.

GlaxoSmithKline reiterated that it did not consider that it had failed to maintain high standards or brought the industry into disrepute. The company denied any breach of Clauses 11.1, 26.1, 26.2, 9.1 and 2 of the Code.

**PANEL RULING**

The Panel noted that LinkedIn was different to some other social media platforms in that it was a business and employment-orientated network and was primarily, although not exclusively, associated with an individual's professional heritage and current employment and interests. In the pharmaceutical industry, the Panel noted that an individual's network might, albeit not exclusively, be directly or indirectly associated with the healthcare industry. In the Panel's view, it was of course not unacceptable for company employees to use personal LinkedIn accounts and the Code would not automatically apply to all activity on a personal account; whether the Code applied would be determined on a case-by-case basis taking into account all the circumstances including: the content, any direct or indirect reference to a product, how the information was disseminated on LinkedIn, the company's role in relation to the availability of the content and whether such activity was instructed or encouraged by the company. If activity was found to be within the scope of the Code, the company would be held responsible.

The Panel noted that the post provided by the complainant was titled 'Looks like another potential vaccines blockbuster!' which appeared in a different font to the rest of the post and was not stated in the linked article. It was not entirely clear to the Panel if this text was added when the post was shared or if it was part of the original post. GlaxoSmithKline made no submission in this regard. This was followed by a picture of a building below which was the statement 'GlaxoSmithKline weighs men B shot Bexsero's promise against gonorrhoea' followed by fiercepharma.com. The Panel noted the complainant's concern that a prescription only medicine was being promoted to the public. The Panel noted that Bexsero was indicated for active immunisation of individuals from 2 months of age and older against invasive meningococcal disease caused by Neisseria meningitidis group B.

The Panel noted that the full article which could be accessed through the website link within the post explained that a study showed that meningitis B vaccines like GlaxoSmithKline's Bexsero could provide some protection against gonorrhea and the company was analysing whether to move forward with testing in the disease area. It further stated that GlaxoSmithKline could not comment further as work remained exploratory and that the company had not yet started any tests in the disease area.

The Panel noted GlaxoSmithKline's submission that the article in question had never been posted or shared on any of its corporate external-facing channels (including GlaxoSmithKline Facebook, YouTube, GlaxoSmithKline LinkedIn or GlaxoSmithKline Twitter).

The Panel noted GlaxoSmithKline's submission that the LinkedIn post in question was shared on LinkedIn by a contract worker engaged by GlaxoSmithKline Global (not GlaxoSmithKline UK Pharma), on their personal LinkedIn account. The Panel noted, however, that the GlaxoSmithKline global headquarters were based in the UK and the contractor who shared the post was based in the UK. The Panel noted GlaxoSmithKline's submission that it played no role in the availability of the content of the post, nor did it instruct or encourage the contractor to disseminate it. According to GlaxoSmithKline, its policies and training made it quite clear to all employees and contractors that

content posted and shared on personal social media accounts risked being perceived as company-endorsed communication, and as such employees and contractor should never post nor share any content that mentioned or referred to prescription medicines other than content that had been specifically approved by GlaxoSmithKline for the general public audience; the contractor in question was trained on the global social media policy and had acted in breach of it.

Contrary to GlaxoSmithKline's submission the Panel did not consider that the issues raised by the complainant required GlaxoSmithKline to train all staff in depth on its product portfolio, but in the Panel's view it was reasonable for it to train all staff on its social media policy which according to GlaxoSmithKline had been done.

In the Panel's view, activity conducted on social media that could potentially alert one's connections to the activity might be considered proactive dissemination of material. In addition, an individual's activity and associated content might appear in that individual's list of activities on his/her LinkedIn profile page which was visible to his/her connections; an individual's profile page was also potentially visible to others outside his/her network depending on the individual's security settings.

The Panel noted that Clause 26.1 prohibited the promotion of prescription only medicines to the public. Clause 26.2 stated that information about prescription only medicines which was made available either directly or indirectly to the public must be factual, presented in a balanced way, must not raise unfounded hopes of successful treatment and must not encourage members of the public to ask their health professional to prescribe a specific prescription only medicine.

The Panel noted that the post itself was headed 'Looks like another potential vaccines blockbuster' and referred to Bexsero as a 'men B shot' and its 'promise against gonorrhea' which was an unlicensed indication. The Panel noted that Bexsero was available as a prescription only medicine in the UK. The Panel further noted that the linked article referred to a study and stated, *inter alia*, 'meningitis B vaccines like GlaxoSmithKline's Bexsero can provide some protection against gonorrhoea ...'.

The Panel did not know how many connections the named contractor had on LinkedIn and if they were all health professionals; the company made no submission in that regard. However, as it was a personal LinkedIn account, the Panel considered that on the balance of probabilities not all the contractor's connections would have been health professionals and therefore sharing of the LinkedIn post and associated article with his/her network constituted promotion of a prescription only medicine to the public and a breach of Clause 26.1 was ruled. The Panel considered that it might encourage members of the public to ask their health professional to prescribe Bexsero and therefore a breach of Clause 26.2 was ruled.

The Panel noted that Clause 11.1 requires that material should only be sent or distributed to those categories of persons whose need for, or interest in, it can reasonably be assumed. The Panel did not consider that the complainant had raised an allegation in this regard and the Panel therefore made no ruling.

The Panel noted its comments and rulings of breaches of the Code as set out above. Overall, the Panel considered that high standards had not been maintained and ruled a breach of Clause 9.1.

The contractor had acted in breach of company policy and training. The Panel considered that the particular circumstances of this case did not warrant a ruling of a breach of Clause 2 of the Code which was a sign of particular censure and reserved for such use. No breach of Clause 2 was ruled.

**Complaint received** **7 December 2018**

**Case completed** **9 August 2019**

**CASE AUTH/3133/12/18**

# ANONYMOUS, NON-CONTACTABLE v NOVO NORDISK

## Declaration of sponsorship of a meeting

**An anonymous, non-contactable individual, who described him/herself as a concerned health professional, complained that a flyer for an International Diabetes Summit which was organised by the All Party Parliamentary Group (APPG) and held at the House of Commons in December 2018 did not have any sponsorship statement despite Novo Nordisk's heavy involvement with the event; its chief executive officer (CEO) was one of the speakers.**

**The complainant alleged that the meeting was advertised across many media channels including websites, social media etc. The complainant alleged numerous breaches of the Code including that there was no evidence of certified meetings.**

**The detailed response from Novo Nordisk is given below.**

**The Panel noted that the Code required that when meetings were sponsored by pharmaceutical companies, that fact must be disclosed in all of the papers relating to the meetings and in any published proceedings. The declaration of sponsorship must be sufficiently prominent to ensure that readers were aware of it at the outset.**

**The Panel noted Novo Nordisk's submission that its CEO was clearly listed on both the flyer and the agenda and that it had made numerous unsuccessful attempts to ensure that a sponsorship statement was included on all relevant materials. The Panel noted email correspondence between Novo Nordisk and the organising office in which the office asked Novo Nordisk to send the line about sponsorship which needed to go in the brochure and Novo Nordisk's recommended wording in response. It was thus unclear why a sponsorship statement had not been used.**

**The Panel noted Novo Nordisk's submission that it had sponsored a panel discussion – Health Inequality in Urban Diabetes; although the APPG had the final decision, Novo Nordisk had suggested the topic for the session and two of the speakers. Novo Nordisk had also paid the speakers' expenses and a fee for service for one of them.**

**Novo Nordisk had also sponsored lunch for the speakers and some attendees, as requested by the APPG for Diabetes.**

**Whilst the Panel noted Novo Nordisk's submission that a verbal declaration was made at the opening of the meeting that elements had been sponsored by Novo Nordisk, Novo Nordisk's sponsorship statement was not included on the information about the meeting on the APPG website or on the meeting flyer provided by the complainant.**

**The Panel noted that a verbal declaration was insufficient and did not negate the failure to include the declaration on the meeting materials. The Panel, therefore, ruled a breach of the Code in relation to each item.**

**The Panel considered that Novo Nordisk had failed to maintain high standards in this regard and a further breach of the Code was ruled.**

**The Panel noted that the Code stated that material relating to medicines and their uses, whether promotional or not, and information relating to human health or diseases which is sponsored by a pharmaceutical company must clearly indicate that it has been sponsored by that company. The Panel noted that the front page of the flyer provided by the complainant included some information about diabetes and a further breach was ruled in this regard due to the lack of sponsorship statement on this material.**

**The Panel considered that the complainant had not established that Novo Nordisk had failed to certify any meetings that required certification under the Code. No breach of the Code was ruled.**

**The Panel noted that the complainant listed a number of other clauses but provided few or no details of why, in his/her view, Novo Nordisk was in breach of those clauses. It was not for the Panel to make out a complainant's allegations. The Panel therefore, ruled no breach of the Code in that regard.**

**The Panel noted that a ruling of a breach of Clause 2 of the Code was a sign of particular censure and reserved for such. In that regard, the Panel did not consider that the particular circumstances of this case warranted such a ruling and no breach of Clause 2 was ruled.**

An anonymous, non-contactable individual, who described him/herself as a concerned health professional, complained about a flyer for an International Diabetes Summit held at the House of Commons in December 2018. The complainant provided a copy of the flyer for the event.

**COMPLAINT**

The complainant noted that the flyer did not have any sponsorship statement although Novo Nordisk was heavily involved with the event; the chief executive officer was one of the speakers and a Team Novo Nordisk rider (cyclist) would attend.

The complainant hoped that such meetings that were held between professionals that abided by such high standards of compliance should be made aware of the involvement of pharmaceutical companies.

The complainant alleged a breach of the Code for sponsored meetings. The complainant alleged that these meetings were advertised across many media channels including websites, social media etc. The complainant alleged breaches of Clauses 2, 9, 14, 18, 19, 20, 22, 23, 24, 26 and 28. With regard to Clause 14, the complainant referred to there being no evidence of certified meetings.

When writing to advise Novo Nordisk, the Authority noted the specific allegations regarding the lack of a statement about the company's involvement in the meeting and in relation to that matter it asked Novo Nordisk to bear in mind the requirements of Clauses 2, 9.1, 9.10, and 22.4.

**RESPONSE**

Novo Nordisk explained that the International Diabetes Summit 2018, held in December 2018 at the House of Commons, was organised by the All Party Parliamentary Group (APPG) for Diabetes. An MP's office organised the meeting in terms of agenda and logistics on behalf of the APPG. An article about the meeting on the APPG website clearly stated that the APPG for Diabetes was holding the meeting, and the contact details for a member of staff in the organising office were given for those wishing to attend.

The Chair of the APPG asked Novo Nordisk to support part of the meeting. The company sponsored the session from 15:15 to 15:55; Panel Discussion – Health Inequality in Urban Diabetes. Novo Nordisk suggested the topic of this session and two of the speakers but the APPG had the final decision on both matters. Novo Nordisk paid travel expenses and accommodation for both speakers, and a fee for service for one of them which was in line with the company's fair market value rates for patients. Accommodation was provided to ensure that both speakers were present for the start of the meeting at 09:30.

Novo Nordisk also sponsored lunch for the speakers and some attendees, as requested by the APPG for Diabetes. The lunch, for 23 people, was by invitation only of the APPG and was held in a private area and the cost was given. This was in line with Novo Nordisk's policy on supporting meetings with similar standards to its own with regard to providing subsistence secondary to education.

The chief executive officer (CEO) of Novo Nordisk A/S (the Head Quarter parent company), attended the meeting and delivered a keynote speech in the afternoon. Novo Nordisk Ltd asked the APPG for Diabetes if the CEO could attend the meeting as he/she was in the UK on that day. The APPG invited the CEO to give a keynote speech. Novo Nordisk had made a significant investment in the UK through the collaboration with Oxford University and the creation of the Oxford Research Centre, therefore Novo Nordisk's support and investment in diabetes research in the UK was of interest to the group. It was clear from the flyer and the agenda that the keynote speaker was the CEO for Novo Nordisk.

Novo Nordisk did not have a list of meeting attendees. There were 11 attendees from Novo Nordisk, including the CEO.

Novo Nordisk communicated with the organising office about the need for a sponsorship declaration on all meeting materials. A member of the market access team had spoken several times to a member of the organising office about the matter and an email was sent with the required wording.

Novo Nordisk explained that Team Novo Nordisk was a diabetes professional cycling team, sponsored by Novo Nordisk A/S. The attendance at the meeting of one of the professional cyclists who was part of the team was arranged by the Region Europe team of Novo Nordisk, based in Copenhagen, Denmark.

Novo Nordisk submitted that it had made numerous attempts to ensure that a sponsorship statement was included on all relevant materials. It was unfortunate that this was not included on the APPG website and flyer provided by the complainant. However, the Chair of the APPG for Diabetes opened the meeting and stated that elements had been sponsored by Novo Nordisk.

Novo Nordisk stated that it tried its best to ensure the sponsorship declaration was included and so it denied a breach of Clauses 9.10 and 22.4. In addition, high standards were upheld and therefore it denied a breach of Clause 9.1. The pharmaceutical industry's reputation was not discredited and therefore Novo Nordisk denied a breach of Clause 2. With regard to the alleged breaches of Clauses 14, 18, 19, 20, 23, 24, 26 and 28, Novo Nordisk did not understand the complainant's concerns as there was no supporting evidence provided. It was unfortunate that the complainant was non-contactable as the company would welcome the opportunity to address any concerns around those clauses. The company was confident that its sponsorship of the meeting was not in breach of those clauses.

**PANEL RULING**

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the PMCPA stated that anonymous complaints would be accepted but that, like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant could not be contacted for more information. The PMCPA was not an investigatory body as such.

The Panel noted that Clause 22.4 stated that when meetings were sponsored by pharmaceutical companies, that fact must be disclosed in all of the papers relating to the meetings and in any published proceedings. The declaration of sponsorship must be sufficiently prominent to ensure that readers were aware of it at the outset.

The Panel noted Novo Nordisk's submission that its CEO was clearly listed on both the flyer and the agenda and that it had made numerous attempts to ensure that a sponsorship statement was included on all relevant materials but unfortunately it was not. The Panel noted email correspondence between Novo Nordisk and the organising office in which the office asked Novo Nordisk to send the line about

sponsorship which needed to go in the brochure and Novo Nordisk's recommended wording in response. It was thus unclear to the Panel why a sponsorship statement had not appeared on the flyer provided by the complainant or the agenda according to Novo Nordisk.

The Panel noted Novo Nordisk's submission that it had sponsored the session from 15:15 to 15:55 titled Panel Discussion – Health Inequality in Urban Diabetes; although the APPG had the final decision, Novo Nordisk had suggested the topic for the session and two of the speakers. Novo Nordisk had also paid travel expenses and accommodation for those two speakers and a fee for service for one of them.

Novo Nordisk had also sponsored lunch for the speakers and some attendees, as requested by the APPG for Diabetes.

Whilst the Panel noted Novo Nordisk's submission that a verbal declaration was made at the opening of the meeting that elements had been sponsored by Novo Nordisk, Novo Nordisk's sponsorship statement was not included on the information about the meeting on the APPG website or on the meeting flyer provided by the complainant. The Panel noted that a verbal declaration was insufficient and did not negate the failure to include the declaration on the meeting materials. The Panel, therefore, ruled a breach of Clause 22.4 in relation to each item.

The Panel considered that Novo Nordisk had failed to maintain high standards in this regard and a breach of Clause 9.1 was ruled.

The Panel noted that Clause 9.10 stated that material relating to medicines and their uses, whether promotional or not, and information relating to human health or diseases which was sponsored by a pharmaceutical company must clearly indicate that it had been sponsored by that company. The Panel noted that the front page of the flyer provided by the complainant included disease information about diabetes and therefore Clause 9.10 was relevant and a breach was ruled.

The Panel noted that the complainant cited Clause 14 and stated that there was no evidence of certified meetings. The Panel noted that the complainant made a general allegation but had not submitted any detailed reasons. The Panel noted that it was not for the Panel to infer detailed reasons to support the allegation on behalf of the complainant. It was for the complainant to establish his/her case on the balance of probabilities. The Panel noted that the complainant bore the burden of proof and considered that he/she had not established that Novo Nordisk had failed to certify any meetings that required certification under the Code. No breach of Clause 14 was ruled.

The Panel noted that the complainant listed a number of other clauses but provided few or no details of why, in his/her view, Novo Nordisk was in breach of those clauses. It was not for the Panel to make out a complainant's allegations. The Panel noted Novo Nordisk's submission that with regard to the alleged breaches of Clauses 18, 19, 20, 23, 24, 26 and 28, it did not understand the complainant's concerns as there was no supporting evidence provided. The Panel, therefore, ruled no breach of Clauses 18, 19, 20, 23, 24, 26 and 28 of the Code.

The Panel noted that a ruling of a breach of Clause 2 of the Code was a sign of particular censure and reserved for such. In that regard, the Panel did not consider that the particular circumstances of this case warranted such a ruling and no breach of Clause 2 was ruled.

**Complaint received** **11 December 2018**

**Case completed** **30 July 2019**

**CASE AUTH/3138/12/18**

# EX-EMPLOYEE v INDIVIOR

## Non-disclosure of transfers of value

**An ex-employee of Indivior complained that in 2017 the company had not disclosed payments made to health professionals, donations or sponsorships in the UK.**

**The detailed response from Indivior is given below.**

**The Panel noted that the Code required companies to document and publicly disclose certain transfers of value made directly or indirectly to health professionals and healthcare organisations located in Europe; in the UK, this had to be via a central platform.**

**The Panel noted Indivior's submission that a previous senior employee had agreed for Indivior to join the list of non-member companies which had agreed to comply with the Code and accept the jurisdiction of the Authority. The Panel was very concerned that this decision had not been more broadly communicated throughout the company; this information only became apparent to those currently employed with the company from April 2019 in relation to this complaint.**

**Indivior was required by the Code, due to its status from June 2017 to disclose 2017 transfers of value to UK health professionals and UK healthcare organisations on the central platform by the end of June 2018, however, the Panel noted that Indivior had failed to do so and therefore it ruled a breach of the Code as acknowledged by the company.**

**The Panel noted Indivior's submission that it had documented all disclosures for 2015 onwards and had (and would) retain those records for at least five years after the end of the calendar year to which they related. The complainant had provided no evidence to the contrary and therefore the Panel ruled no breach of the Code with regard to the retention of data in relation to the 2017 transfers of value.**

**The Panel noted its comments and rulings above and considered that Indivior had failed to maintain high standards and a further breach of the Code was ruled.**

**The Panel noted that Clause 2 was a sign of particular censure and was reserved for such use. Despite Indivior's submission that it had always sought to comply with the spirit of the Code there had been no public disclosure of the 2017 transfers of value on the central platform as required. In the Panel's view, transparency in relation to transfers of value to health professionals and healthcare organisations was of the utmost importance to the reputation of the pharmaceutical industry. The Panel considered, on balance, that Indivior had brought discredit upon and reduced confidence in the industry for its failure to publicly disclose any of its 2017 transfers of value to health professionals and healthcare organisations and it ruled a breach of Clause 2.**

An ex-employee of Indivior, complained that in 2017 the company had not disclosed payments made to health professionals.

**COMPLAINT**

The complainant cited an Indivior website and alleged that in 2017 Indivior decided not to report payments to health professionals, donations or sponsorship in the UK and across Europe unless the countries made their own decisions about reporting. The previous company websites were deleted and so no previous data could be found. No payment had since been reported in the UK. The complainant alleged that this decision was made by named senior executives and supported by others.

The complainant alleged that Indivior had never signed up to being an ABPI member but that it tried to comply with the rules. Not anymore.

When writing to Indivior, the Authority asked it to consider the requirements of Clauses 2, 9.1, 24.1, 24.2, 24.4, 24.5, 24.6 and 24.10 of the 2016 Code in relation to the disclosure of 2016 and 2017 data. The 2015 Code would apply to the disclosure of 2015 data.

**RESPONSE**

Indivior submitted that it had always sought to comply with the spirit of the Code and had appropriately documented transfers of value (copies provided of transfers of values made in 2015, 2016 and 2017). Accordingly, any error that had occurred related only to the disclosure of the data rather than a failure to collect or monitor such transfers of values.

Indivior submitted that in 2015 and 2016, although it was neither a member of the ABPI nor a non-member company that had agreed to comply with the Code and accept the jurisdiction of the PMCPA (a listed non-member), it nonetheless sought to operate in accordance with the spirit of the Code as evidenced by gathering and maintaining data on transfers of values. The company sought to disclose its 2015 data on the ABPI central platform (correspondence was provided). However, it appeared that the correspondence with the ABPI was misinterpreted by Indivior and it mistakenly understood that the data could not be uploaded on to the central platform. Therefore, seeking to comply with the spirit of the Code, the company published the 2015 UK data on its public website. In doing so, an accompanying methodological note (as required by Clause 24.10) was also published on the website (copy provided).

Indivior submitted that due to resourcing and technical challenges, transfers of values for 2016, although collated according to ABPI requirements and in the ABPI template, were not disclosed on the Indivior website. Indivior appreciated that this was inappropriate for a company aligning to the spirit of the Code and that its 2016 transfers of value data should have been disclosed on its website, consistent with the 2015 data disclosure. Nevertheless, whilst this was not in line with the then applicable Code, Indivior did not consider that it was a breach of the Code as, at the time, the company was not a listed non-member and therefore it was not formally subject to the Code and the jurisdiction of the Authority.

Indivior stated that it was not originally aware that a previous senior employee had agreed in June 2017 that the company, although not a member of the ABPI, would, nonetheless, comply with the Code and accept the jurisdiction of the Authority (ie be a listed non-member). The company believed this was done as part of the complaint it raised around that time (Case AUTH/2961/6/17). The company stated that it was regrettable that the previous senior employee did not inform the company more widely at the time so that it was aware of its impact; the company was taking steps to ensure no similar mistakes were repeated. Nevertheless, Indivior only became aware of being a listed non-member company when it was notified of this complaint. However, Indivior stated it had always sought to comply with the Code and, as such, it was happy to accept this status from June 2017 onwards. Under the then applicable 2016 Code, Indivior should thus have disclosed transfers of values in 2017 and in 2018. Further, Indivior should disclose transfers of values in 2018 by the end of June 2019. Consistent with this, Indivior stated that it had documented transfers of value data for 2017 and 2018 in accordance with Code requirements and on the ABPI disclosure template.

Indivior appreciated that from June 2017, it was not only bound to disclose transfers of value data by good intent and seeking to align to the Code, but also obliged to do so as a non-member that had formally agreed to comply with the Code and accept the jurisdiction of the Authority. Accordingly, the company should have disclosed 2017 data in 2018. This did not happen because Indivior was unaware of its membership status.

Indivior noted that since receipt of this complaint, and upon learning that it could use the ABPI central platform it had sought to publish the collated transfers of values data it had on file for 2017 (retrospectively) and 2018 (before the June deadline), and for good practice for 2016 (before it had agreed to comply with the Code and accept the jurisdiction of the Authority) on the central platform.

Indivior noted that the complainant, correctly, referenced that the voluntarily disclosed 2015 data was removed from the company website. Indivior submitted that in early 2018, in seeking to identify a more effective way of managing disclosure of transfers of value data in general, it thought it appropriate to remove old data pending improvements to the disclosure page of its website. This data (including the methodological note) was therefore removed from the company website in March 2018.

Based on interactions with the ABPI, Indivior understood that 2015 data could not now be uploaded and disclosed on to the central platform (as on uploading of 2018 data, 2015 data would naturally fall away). Indivior stated that it would retain the data for 5 years in accordance with Clause 24.6.

Indivior acknowledged that it had failed to disclose 2017 transfers of values made to UK health professionals and healthcare organisations in accordance with the requirements of Clause 24 of the 2016 Code. Thus, it acknowledged breaches of Clauses 24.1 and 24.4.

Given the breaches of Clauses 24.1 and 24.4, Indivior submitted that there were inevitable consequential breaches of Clause 24.5 as the 2017 disclosures were not made available for the requisite three years following disclosure and Clause 24.10 as a methodological note was not published about the 2017 transfers of value.

Indivior submitted that Clause 24.2 appeared as an informative clause in relation to the transfers of values that must be disclosed under Clause 24.1, therefore a breach of that clause was covered by the acknowledged breach of Clause 24.1.

As noted above, in line with Clause 24.6, Indivior submitted that it had documented all disclosures for 2015 onwards and had (and would) retain those records for at least five years after the end of the calendar year to which they related. Therefore, Indivior denied a breach of Clause 24.6. Further, the breaches above would shortly be rectified by the 2017 data being published on the ABPI central platform.

Indivior stated that whilst it strove to maintain high standards, it accepted that it was not aware that a former employee had agreed that Indivior would be a listed non-member company in June 2017 as part of separate proceedings, and most importantly that as a result of this oversight, it had failed to disclose the 2017 data diligently collected in accordance with the Code; these things together could be seen as falling below these standards. However, as noted above, Indivior did collect a comprehensive record of transfers of values and did attempt to voluntarily disclose such data in line with the Code. Indivior was working with the ABPI to use the central platform moving forward to retrospectively publish the 2017 data and publish the 2018 data before the June deadline. The company thus did not consider that it had breached Clause 9.1 of the Code. Moreover, in view of the facts, it did not believe this matter breached Clause 2 of the Code which was reserved for cases of particular censure.

**PANEL RULING**

The Panel noted that Clause 24.1 stated that companies must document and publicly disclose

certain transfers of value made directly or indirectly to health professionals and healthcare organisations located in Europe. The supplementary information to this clause stated that, in the UK, the central platform for disclosure must be used by companies.

Clause 24.2 listed the transfers of value covered by Clause 24.1. Failure to document and publicly disclose transfers of value described in Clause 24.2 would be a breach of Clause 24.1.

The Panel noted Indivior's submission that a previous senior employee had agreed for Indivior to become a listed non-member company and comply with the Code and accept the jurisdiction of the Authority in June 2017, however, this information only became apparent to those currently employed with the company from April 2019 in relation to this complaint. The Panel was very concerned that the decision to join the list of non-member companies which had agreed to comply with the Code had not been more broadly communicated throughout the company.

The Panel noted Indivior's submission that its 2015, 2016 and 2017 transfers of value data were not disclosed on the central platform required by the Code in the UK. The Panel noted, however, that as Indivior only became a listed non-member company which had agreed to comply with the Code and accept the jurisdiction of the Authority from June 2017, the requirement to disclose the 2015 and 2016 ToVs on the central platform did not apply to Indivior and the Authority could make no ruling in relation to the disclosure of such data under the Code.

Indivior was required by the Code, due to its status from June 2017 as a listed non-member company which had agreed to comply with the Code and accept the jurisdiction of the Authority, to disclose 2017 ToV to UK health professionals and UK healthcare organisations on the central platform by the end of June 2018, however, the Panel noted that Indivior had failed to do so and therefore it ruled a breach of Clauses 24.1 and 24.4 as acknowledged by the company.

The Panel considered that as there had been no public disclosure of the 2017 transfers of value at the time the Authority received the complaint, Clauses 24.5 and 24.10 were not relevant and no ruling was made in that regard.

The Panel noted Indivior's submission that it had documented all disclosures for 2015 onwards and had (and would) retain those records for at least five years after the end of the calendar year to which they related. The complainant had provided no evidence to the contrary and therefore the Panel ruled no breach of Clause 24.6 in relation to the 2017 data. The Panel noted its comments and rulings above and considered that Indivior had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted that Clause 2 was a sign of particular censure and was reserved for such use. The Panel noted that despite Indivior's submission that it had always sought to comply with the spirit of the Code there had been no public disclosure of the 2017 transfers of value on Indivior's website. The Panel further noted that there had been no public disclosure of the 2017 transfers of value on the central platform as required by the Code. In the Panel's view, transparency in relation to transfers of value to health professionals and healthcare organisations was of the utmost importance to the reputation of the pharmaceutical industry. The Panel considered, on balance, that Indivior had brought discredit upon and reduced confidence in the industry for its failure to publicly disclose any of its 2017 transfers of value to health professionals and healthcare organisations and it ruled a breach of Clause 2.

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| **Complaint received** | **20 December 2018** |
| **Case completed** | **19 August 2019** |

**CASE AUTH/3148/1/19**

# COMPLAINANT v GLAXOSMITHKLINE

## Online promotion of Seretide

**A complainant who described him/herself as a concerned UK health professional, complained about a Seretide Evohaler (fluticasone/salmeterol) advertisement in Pulse, which he/she had accessed via an iPad and a laptop.**

**The complainant noted that he/she could not see the ingredients of Seretide at the top of the advertisement. He/she noted that it might be below the product logo at the bottom of the advertisement, but it was not legible; it was no better on a laptop screen.**

**The detailed response from GlaxoSmithKline is given below.**

**The Panel noted that the electronic advertisement consisted of four frames.**

**It was not clear whether the complainant had viewed the four frames and taken a screen shot of frame 2 or had only seen frame 2 due to technical issues which came to GlaxoSmithKline's attention following the complaint. The third party agency, unbeknown to GlaxoSmithKline, had arranged for frame 2 to be the static 'back up' frame that would be shown if there were problems with digital material when viewed on certain browsers. The Panel considered that the 'back up' frame was in effect a separate advertisement for some viewers and thus should be treated as such. The Panel decided to rule on each advertisement separately.**

**The Panel noted that frame 1 of the four frame advertisement included the non-proprietary name immediately adjacent to the first appearance of the brand name and this was legible and thus the Panel ruled no breach of the Code.**

**In relation to the advertisement which consisted solely of frame 2, the Panel noted that frame 2 included the product name twice, once as a heading and secondly as part of the brand logo at the bottom of the frame. The non-proprietary name was given but it was not immediately adjacent to the first appearance of the brand name and its appearance as part of the brand logo was not readily readable. The Panel therefore ruled a breach of the Code.**

**The Panel ruled no breach of the Code as GlaxoSmithKline had not failed to maintain high standards.**

A complainant who described him/herself as a concerned UK health professional, complained about a Seretide Evohaler (fluticasone/salmeterol) advertisement in Pulse, which he/she had accessed via an iPad and a laptop.

Seretide was marketed by GlaxoSmithKline and indicated for use in the treatment of asthma. The advertisement at issue highlighted a 50% reduction in the list price.

**COMPLAINT**

The complainant noted that he/she could not see the ingredients of Seretide at the top of the advertisement. He/she noted that it might be below the product logo at the bottom of the advertisement, but it was not legible; it was no better on a laptop screen.

When writing to GlaxoSmithKline, the Authority asked it to consider the requirements of Clauses 4.3 and 9.1.

**RESPONSE**

GlaxoSmithKline noted that the complaint was about a dynamic digital banner advertisement for Seretide (ref UK/SFC/0010/18b), placed in the digital edition of Pulse, in December 2018. The purpose of the advertisement was to remind health professionals of the legacy of Seretide and to inform them of the 50% price reduction.

Seretide was the first inhaled corticosteroid/long-acting beta-agonist (ICS/LABA) available in the UK in February 1999, so its brand name and active ingredients were generally well known amongst health professionals.

The dynamic digital banner advertisement at issue was made up of four rotating frames which appeared in sequential order. The banner advertisement always started with the first frame. Each frame was visible for three seconds which made the whole advertisement twelve seconds long.

The item was certified as a dynamic digital banner advertisement only, with the timings of each frame included in the gallery of the job bag as well as the landing page where the dynamic digital item could be viewed, and the medical signatory specifically stated that he/she had viewed the final form item when signing the second signature box.

As per in-house guidance on banner advertisements, the size of the non-proprietary name was checked and was found to be legible. The unique job bag identifier was also checked and appeared on the fourth frame. Pdf copies for the digital advertisement as seen by the final signatory were provided.

GlaxoSmithKline stated that it was surprised to receive the complaint as the item had been certified in good faith and in accordance with internal

procedures, which were based on the Code as it related to digital materials.

GlaxoSmithKline submitted that it investigated where or how a single frame of the advertisement could appear in Pulse. This included discussion with its third party media planning and buying agency which was involved in the distribution of this item.

At a telephone conference in January 2019, the third party agency told GlaxoSmithKline that occasionally there might be issues with digital material when viewed by individuals using certain (generally old) browsers. To allow for this, its standard policy was to have a 'back-up' image that the reader viewed should this occur. The agency decided to use the second of the four frames as this 'back-up' frame, without informing GlaxoSmithKline. The job bag was, therefore, certified in the belief by both the originator and final signatory that it was a dynamic digital banner advertisement which always started with the first frame (with the larger non-proprietary name written on it) and which then continued in a sequential fashion through to the end, where the unique job bag identifier was located.

At the January telephone conference, the nature of the complaint was also discussed and how it could have occurred. It was thought that the complainant might have taken a screenshot of frame 2 as part of the dynamic banner advertisement as he/she was scrolling through the frames, or he/she might have just seen the static 'back-up' frame, (frame 2). Frame 2 had the much smaller non-proprietary name associated with the logo and no job bag identifier. The agency stated that it was impossible to know for certain which of these two options could have been the cause without further information on the complainant's browser capabilities when the screenshot was taken.

The agency acknowledged that the selection of the second frame, without any prior discussion or consultation with GlaxoSmithKline, was an error on its behalf and it had taken full responsibility. Further to this complaint, the agency had now changed its process such that all 'back-up' images were left blank, unless an approved static banner was provided.

GlaxoSmithKline stated that it had certified the dynamic digital banner advertisement in good faith and in line with the Code as it related to digital material. Those who developed and approved the item were unaware of the technical difficulties that might occur when dynamic digital materials were viewed by different browsers or what an agency might do to mitigate these. Neither the job bag originator nor the medical signatory had further qualifications in information technology and so it was not unreasonable for them to be unaware of these complexities.

The first frame of the certified item started with the words 'Remember your first success story with Seretide', had the non-proprietary names (salmeterol/fluticasone propionate) clearly written directly after this first mention of the brand name, in line with the supplementary information for Clause 4.1 relating to electronic journals. Clause 4.3 contained similar information but was less detailed as far as the guidance for digital materials was concerned. GlaxoSmithKline confirmed that the non-proprietary name was appropriately placed (on the first frame), was clearly readable and complied with the guidance given in Clause 4.3 relating to digital material. Furthermore, the size of the non-proprietary information complied with the general information given in Clause 4.3 which was originally devised for hard copy materials as the non-proprietary name of 32 characters occupied a total area which was similar in size to the brand name 'Seretide' which was only 8 characters as officially measured by Pulse.

The unique identifier for the job bag was include in frame 4.

GlaxoSmithKline therefore denied any breach of Clause 4.3.

GlaxoSmithKline noted that each of the 4 frames of the banner advertisement had, at the bottom of them, the same brand logo for Seretide. The brand logo had the accompanying non-proprietary name written directly below it. The constraints relating to the non-proprietary names did not apply to brand logos, as this was neither the first, nor the most prominent mention of the brand name. The Seretide dynamic digital banner advertisement mentioned the non-proprietary name four times, twice on the first frame and each time on frames 2, 3 and 4.

GlaxoSmithKline did not consider that it had failed to maintain high standards. The item in question was certified according to Clause 14 and there was clear communication between GlaxoSmithKline and the agency about the use of the dynamic digital banner advertisement. It was also unclear as to whether the complainant saw this as a frame of the dynamic digital banner advertisement or as a static digital banner advertisement which the agency had developed and which at the time of placement, had not been developed by the creative department within GlaxoSmithKline for certification. However, the non-proprietary name was present as part of the Seretide brand logo.

GlaxoSmithKline noted that there was no case precedent where an alleged breach of Clause 4.3 had by itself been associated with an alleged breach of Clause 9.1 and that failure to provide legible non-proprietary information and a unique job bag identifier under the circumstances outlined would reflect failure to maintain high standards. GlaxoSmithKline thus denied a breach of Clause 9.1.

**PANEL RULING**

The Panel noted that the electronic advertisement consisted of four frames.

It was not clear whether the complainant had viewed the four frames and taken a screen shot of frame 2 or had only seen frame 2 due to technical issues which came to GlaxoSmithKline's attention following the complaint. The third party agency, unbeknown

to GlaxoSmithKline, had arranged for frame 2 to be the static 'back up' frame that would be shown if there were problems with digital material when viewed on certain browsers. The Panel considered that the 'back up' frame was in effect a separate advertisement for some viewers and thus should be treated as such. The Panel decided to rule on each advertisement separately.

The Panel noted that frame 1 of the four frame advertisement included the non-proprietary name immediately adjacent to the first appearance of the brand name and this was legible. Thus the Panel ruled no breach of Clause 4.3 of the 2016 Code in relation to the four frame advertisement.

In relation to the advertisement which consisted solely of frame 2, the Panel noted that frame 2 included the product name twice, once as a heading and secondly as part of the brand logo at the bottom of the frame. The non-proprietary name was given but it was not immediately adjacent to the first appearance of the brand name and its appearance as part of the brand logo was not readily readable. The Panel therefore ruled a breach of Clause 4.3 of the 2016 Code.

The Panel did not consider that the circumstances were such that GlaxoSmithKline had failed to maintain high standards and thus ruled no breach of Clause 9.1 of the 2016 Code.

GlaxoSmithKline appealed the Panel's ruling of a breach of Clause 4.3 of the Code. This was withdrawn by GlaxoSmithKline prior to consideration by the Appeal Board.

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| **Complaint received** | **9 January 2019** |
| **Case completed** | **20 May 2019** |

**CASE AUTH/3151/1/19**

# ANONYMOUS EMPLOYEES v OTSUKA EUROPE

## SPC changes and prescribing information

**A 'group of concerned employees' complained that Otsuka Pharmaceuticals Europe Ltd (based in the UK) was unable to properly manage updates to the summary of product characteristics (SPC) and prescribing information for Jinarc (tolvaptan). Jinarc was used in certain patients with chronic kidney disease.**

**The complainants alleged that the latest SPC and prescribing information update for Jinarc took place on 21 December 2018, and emails sent out for action/information indicated that the process was in chaos. Senior members of the European team did not appear to understand the process.**

**The complainants were saddened that even after having received a complaint in June 2018 [Case AUTH/3041/6/18] and further concerns at the end of last year, Otsuka Europe seemed unable to put this critical process concerning patient safety in place.**

**At an EU medical meeting a senior employee stated that he/she knew that the new standard operating procedure (SOP) (MA 002) for updating SPCs and prescribing information was flawed, but it was still approved and sent out for training, as he/she wanted to 'test the affiliates'. Moreover, he/she added that Otsuka could perhaps use legal privilege to prevent the PMCPA receiving all the necessary information. The complainants queried whether the content of any response from Europe could be trusted and alleged that the European organization was compromised.**

**In subsequent communication, the complainants raised more concerns about Otsuka Europe and Otsuka Europe Development and Commercialisation (D&C) Ltd.**

**The complainants noted their concern about communication from Otsuka Europe D&C regarding information about Jinarc Type IA-IN-G (addition of wallet card blister) European Medicines Agency (EMA) favourable opinion dated 21 December 2018 and noted that global medical had been kept in the loop of such communication. The complainants queried what the Japanese global headquarters had done to rectify the situation. Members of the global quality, regulatory and safety (QRS) team were copied into the emails; were they not aware that the current situation was unacceptable?**

**The complainants noted that some people copied into the email had left the business. What checks had been done to ensure the appropriate staff members received this important notification if the mailing lists were not kept up-to-date?**

**The complainants gave key dates with regard to changes to the Jinarc package information and alleged that the date for new/updated SPC and package leaflets to be distributed was wrong. If Otsuka Europe and Otsuka Europe D&C could not calculate the dates appropriately, what were the affiliates and third parties supposed to do?**
**The complainants alleged that out-of-date Jinarc prescribing information (prepared December 2018) had the incorrect stages for chronic kidney disease – it should have stated stages 1 to 4 and not 1 to 3. There were also missing adverse events – the complainants provided a track change copy of the prescribing information.**

**The complainants stated that there was no central repository for storing up-to-date prescribing information. Moreover, there was no standard process for creating the prescribing information. This increased the risk of the incorrect document/ lack of standardized prescribing information across the brands and incorrect timelines distributed to the affiliates and third parties.**

**The complainants stated that the correct prescribing information was distributed on 10 January 2019 with the correct indication and safety updates.**

**The complainants were very concerned that the process for the distribution of SPCs and prescribing information was still not correct despite the new SOP which came into effect at the end of October 2018. The process was not fit for purpose and was currently being rewritten by medical. If the process was not ready/correct, it should not have been trained out to the entire European organization.**

**The complainants stated that there was a prevalent blame culture within the organization. There was a climate of fear within the European organisation and the complainants believed that senior leaders within Otsuka Europe and Otsuka Europe D&C were lining up their next sacrificial lambs as the process was still not fit for purpose.**

**The complainants were also saddened that the global QRS team and the Japanese headquarters had failed to take a more involved approach. This was a critical process that impacted patient safety, and it had not been given the priority it deserved.**

**The detailed response from Otsuka Europe is given below.**

**The Panel noted Otsuka Europe's submission that the SPC update in question related to the addition of blisters in wallet cards with new marketing authorization holder (MAH) numbers. The Panel noted that the communication in question, dated 21 December 2018, included several required affiliate actions including timelines for, *inter alia*, distribution of the updated SPC and package leaflet, withdrawal**

**of previous SPC, package leaflet and promotional materials and update of non-promotional materials. The Panel noted that the timeline for actions were given in both the number of business days and the completion date. The Panel noted that there was some confusion in that the number of business days did not appear to correlate with the completion date.**

**The Panel noted Otsuka Europe's submission that the timelines stipulated in the communication in question were calculated incorrectly and caused some affiliates to question the dates provided. The Panel considered, however, that the completion dates in the email in question appeared to be correct if 24 and 31 December and the public holidays were not considered to be working days. The Panel was concerned to note that these specific/ additional 'non-working days' did not appear to be either covered in the relevant SOP or to be widely communicated and, in the Panel's view, this caused confusion as had an incorrect reference to the communication in question as 'the Jinarc SmPC change regarding gout', which was not so.**

**The Panel noted that although a completion date was given, the confusion around how the dates were calculated (with regard to business days) and the lack of clear communication in this regard caused confusion with regard to a critical process and meant that Otsuka Europe had failed to maintain high standards. A breach was ruled.**

**The Panel did not consider that the email demonstrated that senior European leaders did not understand the process and no breach was ruled in this regard.**

**With regard to the incorrect prescribing information included in the communication in question, the Panel noted Otsuka Europe's timeline of events; the SPC was revised in July 2018 to include an extension to the indication in Section 4.1 (CKD stage 4) and the addition of abdominal pain as a common side effect to Section 4.8; the prescribing information was updated at the time to reflect these SPC changes. There was then a further SPC change regarding the addition of acute liver failure to Sections 4.4 and 4.8 which were included in the revised September 2018 prescribing information. In November 2018, the SPC due to a change of marketing authorisation holder and again in December 2018 to include the addition of wallet card blisters. Both the November 2018 and December 2018 prescribing information omitted the previously added information regarding CKD stage 4, abdominal pain and acute liver failure.**

**The Panel noted the requirements for prescribing information (defined by Clause 4.2) including that it must be up-to-date and must be consistent with the SPC for the medicine. The Panel noted Otsuka Europe's submission that, although certified and distributed to affiliates, neither the November 2018 nor the December 2018 prescribing information was used in external materials. The Panel was unclear with regard to what Jinarc promotional material, if any, was in circulation during November and December. Otsuka Europe made no submission in this regard. The Panel noted that the complaint concerned the internal distribution of the Jinarc prescribing information dated December 2018 as an attachment to the email dated 21 December 2018; the complainant made no reference to its use on materials. The Panel considered that it had no evidence before it in this case that incorrect or out-of-date prescribing information was actually used and considered that there was no allegation concerning its use on materials and in that regard, ruled no breach. The Panel noted that the use of incorrect Jinarc prescribing information on materials was the subject of another complaint (Case AUTH/3041/6/18).**

**Although it appeared that the errors in the December 2018 prescribing information had been identified internally prior to the Authority's receipt of the complaint and remedial action taken, the Panel considered that Otsuka Europe had failed to maintain high standards by certifying and distributing incorrect prescribing information which omitted important safety information and a change to the licensed indication and which had the potential to be used in multiple affiliates. A breach of the Code was ruled.**

**The Panel noted Otsuka's submission that it was developing a repository and a process for authoring/ updating prescribing information, however, this was not currently in place. The Panel was concerned that there appeared to be a general lack of oversight and guidance with regard to prescribing information creation and revision and noted the errors that had occurred in the November and December 2018 Jinarc prescribing information. Prescribing information was critical information required in all promotional materials and had the potential to impact patient safety. The Panel noted that Otsuka acknowledged that the relevant SOP still needed to be improved in relation to both SPC and prescribing information updates. The Panel considered that the lack of a clear process for both the creation and revision of prescribing information and SPC updates meant that Otsuka Europe had failed to maintain high standards and a breach was ruled.**

**The Panel noted that the complainants had provided no evidence that individuals who should have received the communication in question had been omitted from the distribution list. That the email in question had been sent to individuals who had left the company was not in itself a breach of the Code so long as individuals who should have received it had done so. In the Panel's view, the complainants had not discharged their burden of proof to show that a breach of the Code had occurred in this regard and no breach was ruled.**

**The Panel noted the complainants' allegations that a senior member of the Otsuka Europe medical team stated that the SOP for SPC and prescribing information updates was flawed but was still approved and trained out in order to 'test the affiliates'; and that he/she stated that Otsuka Europe could use legal privilege to prevent the PMCPA receiving all the necessary information. The Panel noted that Otsuka Europe found no evidence that these statements were made. It appeared that there had been an acknowledgement at the meeting in question that the SOP required improvement. One**

**person recalled use of the word 'flawed'. Otsuka Europe acknowledged that the SOP required improvement. The Panel considered that this was a serious allegation; self-regulation relied upon, *inter alia*, full transparency from companies. The parties' accounts differed. It was difficult to determine where the truth lay. The Panel noted, however, that the complainants bore the burden of proof and considered, on balance, that the burden of proof had not been discharged and it therefore ruled no breach.**

**With regard to the allegations about the Japanese parent company, global quality, regulatory and safety team, global medical and pharmacovigilance, the complainants had provided no detail and, in the Panel's view, the complainants had not discharged their burden of proof. No breach was ruled in this regard.**

**With regard to the allegation that there was a prevalent blame culture within the organisation and a climate of fear, the Panel considered that comments about the culture of an organisation might fall within the scope of the Code if that culture directly or indirectly contributed to a breach of the Code. The Panel noted Otsuka's submission that Otsuka Europe had a whistleblowing procedure and an incident response procedure which specifically stated that employees would be protected from retaliation. The complainants had provided no detail with regard to this allegation and, in the Panel's view, the complainants had not discharged their burden of proof. No breach was ruled in this regard.**

**The Panel noted its comments and rulings above. The Panel noted that Clause 2 was a sign of particular censure and reserved for such use. On balance, the Panel did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 and ruled no breach accordingly. This ruling was appealed by the complainants.**

**The Appeal Board noted from the Panel's rulings above that there was a lack of clear process for both the creation and revision of prescribing information and SPC updates; that Otsuka Europe had certified and internally distributed to multiple affiliates incorrect prescribing information which omitted important safety information and a change to the licensed indication; and that the lack of clear communication about completion dates for an SPC update caused confusion with regard to a critical process had meant that Otsuka Europe failed to maintain high standards and three separate breaches of the Code were ruled.**

**The Appeal Board noted that Otsuka Europe agreed with the complainants' appeal that the cumulative effect of the issues warranted a breach of Clause 2. The company apologised for its inability to effectively remediate the issues highlighted in Case AUTH/3041/6/18, and its continued failure to address the issues with regard to SPC updates and prescribing information. Otsuka Europe submitted that these failings had reduced confidence in the pharmaceutical industry. The Appeal Board was very concerned about how long it was taking Otsuka Europe to address these issues. Otsuka Europe stated that this delay was due to the company failing to understand the role of prescribing information in relation to patient safety.**

**The Appeal Board considered that the cumulative effect of Otsuka Europe's failings in this case reduced confidence in the pharmaceutical industry and ruled a breach of Clause 2. The appeal on this point was successful.**

A 'group of concerned employees' complained that Otsuka Pharmaceuticals Europe Ltd (based in the UK) was unable to properly manage updates to the summary of product characteristics (SPC) and prescribing information for Jinarc (tolvaptan). Jinarc was used in certain patients with chronic kidney disease.

**COMPLAINT**

The complainants stated that during the recent EU medical meeting, they were informed that Otsuka had received a further complaint about the update of SPCs and prescribing information at the end of 2018.

The complainants submitted that the latest SPC and prescribing information update for Jinarc took place on 21 December 2018, and emails sent out for action/information indicated that the process was in chaos. Communication from senior members of the European team demonstrated that they did not understand the process.

The complainants were saddened that even after having received a complaint in June 2018 [Case AUTH/3041/6/18] and further concerns at the end of last year, Otsuka Europe seemed unable to put this critical process concerning patient safety in place.

At the EU medical meeting referred to above, a senior employee stated that he/she knew that the new standard operating procedure (SOP) (MA 002) for updating SPCs and prescribing information was flawed, but it was still approved and sent out for training, as he/she wanted to 'test the affiliates'. Moreover, he/she added that Otsuka could perhaps use legal privilege to prevent the PMCPA receiving all the necessary information. The complainants queried whether the content of any response from Europe could be trusted if this was the view of a senior member of the team. The complainants considered that the European organization was compromised.

In subsequent communication, the complainants raised more concerns about Otsuka Europe and Otsuka Europe Development and Commercialisation (D&C) Ltd.

The complainants noted their concern about communication from Otsuka Europe D&C regarding information about Jinarc Type IA-IN-G (addition of wallet card blister) European Medicines Agency (EMA) favourable opinion dated 21 December 2018 and noted that global medical had been kept in the loop of such communication. The complainants queried what the Japanese global headquarters had

done to rectify the situation, especially as it must be aware of the numerous failings in the process (especially since June 2018). If Otsuka Europe and Otsuka Europe D&C had failed to distribute SPC and prescribing information appropriately, did Japan not take note and act accordingly? What actions, if any, did Japan take to help or rectify the situation? The complainants stated that they could not ask such questions in their organization for fear of retribution. Members of the global quality, regulatory and safety (QRS) team were copied into the emails; were they not aware that the current situation was unacceptable? The complainants had heard that the global QRS team had been kept updated by senior leaders in Otsuka Europe and was satisfied with the progress – surely this could not be the case. This made a mockery of patient safety if the global QRS team had done little or nothing to correct the European processes.

The complainants noted that some people (names provided) copied into the email left the business in the summer of 2018; they had been part of the team that was supposed to rewrite the process for SPC and prescribing information distribution. What checks had been done to ensure the appropriate staff members received this important notification if the mailing lists were not kept up-to-date?

The complainants gave key dates with regard to changes to the Jinarc package information and alleged that the date for new/updated SPC and package leaflets to be distributed was wrong – within 2 business days due 28 December 2018, but if the start date for implementation was 19 December 2018 (as stated on page 1 of the relevant document) 2 business days was 21 December 2018, or if the start date for implementation was 21 December 2018, 2 business days was 24 December 2018. The implementation dates for withdrawal of the SPC were also alleged to be wrong – 5 business days, due by 4 January 2019 but if the start date for implementation was 19 December 2018, 5 business days was 27 December 2018 and if the start date for implementation was 21 December 2018, 5 business days was 31 January [sic].

The complainants stated that it was very confusing as there seemed to be additional days that had not been counted, apart from the public holiday. If Otsuka Europe and Otsuka Europe D&C could not calculate the dates appropriately, what were the affiliates and third parties supposed to do?

The complainants alleged that out-of-date Jinarc prescribing information (prepared December 2018) had the incorrect stages for chronic kidney disease – it should have stated stages 1 to 4 and not 1 to 3. There were also missing adverse events – the complainants provided a track change copy of the prescribing information to illustrate the point.

The complainants stated that there was no central repository for storing up-to-date prescribing information. Moreover, there was no standard process for creating the prescribing information. The complainants considered that this increased the risk of the incorrect document/lack of standardized prescribing information across the brands and incorrect timelines distributed to the affiliates and third parties.

The complainants stated that the correct prescribing information was distributed on 10 January 2019 with the correct indication and safety updates (copy provided).

The complainants were very concerned that the process for the distribution of SPCs and prescribing information was still not correct despite the new SOP which came into effect at the end of October 2018. The process was not fit for purpose, as stated above and was currently being rewritten by medical from scratch. If the process was not ready/correct, it should not have been trained out to the entire European organization.

The complainants stated that there was a prevalent blame culture within the organization. A senior employee was removed from the business because he/she was blamed for not correcting the SOP in time. There was a climate of fear within the European organisation and the complainants believed that senior leaders within Otsuka Europe and Otsuka Europe D&C were lining up their next sacrificial lambs as the process was still not fit for purpose.

The complainants were also saddened that the global QRS team and the Japanese headquarters had failed to take a more involved approach. This was a critical process that impacted patient safety, and it had not been given the priority it deserved.

When writing to Otsuka Europe, the Authority asked it to consider the requirements of Clauses 4.1, 4.2, 9.1 and 2 of the 2016 Code.

**RESPONSE**

Otsuka Europe noted that the complainants referred to the update to the Jinarc SPC and prescribing information that it sent out on 21 December 2018 for the addition of blisters in wallet cards with new Marketing Authorization Holder (MAH) numbers. The complainants specifically alleged that:

- the emails sent out for action indicated that the process (EU-SOP-MA-002) was in chaos;
- emails from senior European leaders demonstrated a lack of understanding of the process; and
- the prescribing information communicated on 21 December 2018 was incorrect as it did not have all the necessary safety information.

Otsuka Europe disagreed that the communication sent indicated that the process was in chaos or demonstrated a lack of understanding of the process, despite demonstrating opportunities to improve the process. However, the complainants were correct in their more important claim; the prescribing information sent out on 21 December 2018 was inconsistent with the revised SPC as it did not have all the necessary safety information. This prescribing information, however, was not used and in that regard the company denied a breach of Clauses 4.1 and 4.2.

Otsuka Europe submitted that, additionally, on 21 February 2019 it identified discrepancies between the January 2019 version of the Jinarc prescribing information and the current SPC, some of which were present at least as far back as 30 July 2018 (corresponding SPC and prescribing information revisions were provided). On 21 February 2019, out of an abundance of caution, an employee recalled the February 2019 prescribing information which included these same discrepancies. These discrepancies were escalated through the Otsuka governance process documented in PV-3101-GSOP 'Safety Governance' to the medical safety review team, which evaluated the potential for a risk to patient safety. This team was the main global governance body responsible for the overall management of safety issues related to all Otsuka pharmaceutical products (both marketed and in development). Over the course of two meetings, held on 22 and 23 February 2019, the medical safety review team reviewed the January Jinarc prescribing information and determined that the discrepancies noted with the approved SPC did not pose a risk to patient safety. In particular, the evaluation of the phrasing 'should' vs 'must' in relation to having access to, and being able to drink sufficient amounts of water, was reviewed. The review team concluded that there was no inconsistency between the SPC and the January prescribing information on that point.

Otsuka Europe submitted that, based on the conclusion of the medical safety review team, it had considered these discrepancies against the requirements of Clauses 4.1 and 4.2 of the Code. Although the version of the prescribing information that was distributed contained discrepancies with the latest approved SPC, it remained consistent as a condensed version of the SPC. Specifically, common adverse reactions and serious adverse reactions likely to be encountered in clinical practice as well as precautions and contra-indications were appropriately described. Therefore, Otsuka Europe concluded that these discrepancies were not in breach of Clauses 4.1 or 4.2 (Otsuka Europe provided a timeline of relevant events).

Otsuka Europe submitted that, in both the November and December prescribing information revisions, the overall process did not prevent prescribing information which was inconsistent with the SPC from being certified and communicated to affiliates. Additionally, the overall process did not detect and resolve differences in opinion related to discrepancies between the SPC and prescribing information as identified on 21 February 2019. Therefore, despite efforts to remediate the issues highlighted in Case AUTH/3041/6/18, the company was not effective in doing so. As this was a continued failure to address the issues originally described in Case AUTH/3041/6/18, Otsuka Europe acknowledged a breach of Clauses 9.1 and 2. As EU-SOP-MA-002 had not effectively achieved a key objective, ie to ensure that up-to-date prescribing information was provided when performing promotional activities, the company acknowledged a further breach of Clauses 9.1 and 2.

Otsuka submitted that it had assessed these failings and identified contributing factors, with their associated remediations which it would address as a matter of urgency (details provided).

Otsuka Europe submitted that it regretted and apologised for the slow progress it had made in this regard. The remediations identified were under way. Additionally, an independent audit, to be conducted from 25 February to 1 March 2019, would assess the entire end-to-end product labelling process including the medical affairs segment. Any findings which were identified would be included in the remediation programme.

Otsuka Europe noted that there had been successes in its remediations: notifications of changes to SPC and prescribing information were sent to all affiliates via general mailbox addresses; tracking the implementation of prescribing information changes (including withdrawal of promotional material) was in place and the company had shortened its windows to withdraw promotional material.

Otsuka Europe noted that the complainants had also referred to a recent EU medical meeting at which it was alleged that a senior employee commented on the current version (version 5) of EU-SOP-MA-002 and also on the provision of information to the PMCPA. Given the date of the complainants' letter and its receipt by the PMCPA, it was possible that the complainants had referred to one of two meetings that took place in January 2019; details were provided.

Otsuka submitted that attendees of both meetings had been interviewed. Otsuka Europe had interviewed relevant individuals and the interview notes were provided.

A number of those interviewed recalled a general agreement that the current version of EU-SOP-MA-002 could be improved but there was no evidence that a senior employee stated that, in general, the SOP was flawed or that it was being trained out to test affiliates. One interviewee recalled the word 'flawed' being used, but only in the context of the need to remove the requirement and timelines for the reintroduction of revised promotional material. The senior employee might have referred to improving the SOP once it had been used in practice, but, given that processes should be regularly reviewed with a view to continuous quality improvement, the company did not consider that this was inappropriate or in breach of the Code. There was no evidence that any comment was made at either meeting about using legal privilege to prevent information being received by the PMCPA and Otsuka Europe denied any breach of the Code in that regard.

Otsuka Europe noted that the complainants had raised a number of other concerns:

- Oversight from the global organisation and distribution of information as well as maintenance of the email lists used to notify affiliates of SPC and prescribing information changes;
- Confusion in relation to timelines;

- Out-of-date prescribing information (addressed above);
- Distribution of correct prescribing information (addressed above); and
- Concern about the relevant process and blame culture.

Otsuka Europe refuted the complainants' allegations that it did not provide information or receive oversight from the global organisation; while the company could improve its email list maintenance, the existing process to update mailing lists did not constitute a breach of the Code. Otsuka Europe recognized that despite its best efforts to remediate, EU-SOP-MA-002 still needed to be improved as there continued to be inconsistencies between the SPC and prescribing information. Otsuka Europe also recognized that while many employees used internal reporting mechanisms to raise matters of concern, some at least felt uncomfortable doing so.

**Oversight from the global organisation and distribution of information**

Otsuka Europe noted the complainants' concern that global medical and the global QRS team might not have been kept fully informed in relation to the issues faced by Otsuka Europe to communicate to affiliates changes to SPCs or might not have taken any action in relation to such issues. Otsuka Europe confirmed that there had been significant communication within Otsuka in relation to the issues via a number of channels:

1 Updates on remediation progress by members of Otsuka Europe senior leadership and compliance to the Otsuka Europe Board on a quarterly basis.
2 At least a dozen updates including both remediation progress and complaint response updates to the global QRS team, as PMCPA complaints had been received and responses drafted by Otsuka Europe.
3 Ad hoc updates via the emergency compliance risk reporting route to Otsuka Pharmaceutical Company Compliance, as PMCPA complaints had been received and responses drafted by Otsuka Europe.
4 Monthly remediation progress updates from senior Europe employees. This was implemented as a recommendation of the Otsuka Europe Board.

Details about vanity roles were provided including that the global QRS team was the overarching global governance, decision-making and oversight body for significant quality, regulatory, and safety issues. The team had been quite involved in providing recommendations and suggestions to Otsuka Europe during a dozen planned and ad-hoc meetings since June 2018. In addition, on 31 January 2019, it approved an independent audit to provide a comprehensive and objective assessment of the entire end-to-end labelling process, with a plan for accelerated remediation of all findings and observations. This audit planned to identify and holistically address the gaps in the process and took place from 25 February through to 1 March 2019.

The Otsuka Europe board had told Otsuka Europe that the remediation was moving too slowly and it asked Otsuka Europe to work with global regulatory affairs, global pharmacovigilance and global quality through Otsuka Europe D&C to speed up the corrective actions. Additionally, the Otsuka Europe board recommended monthly updates from a named employee at Otsuka Europe to a very senior employee in medical, safety, regulatory and quality.

Otsuka Europe noted that regardless of the recommendations and advice received from global, it was ultimately responsible for the successful execution of the plans to improve the processes that required remediation, in addition to communicating up-to-date and appropriate information on its marketed products to prescribers.

In summary, Otsuka Europe refuted the allegation that the global organisations had failed to take a more involved approach over issues related to the SPC implementation process. There had been consistent oversight, communication and provision of advice where considered appropriate as noted above. However, not all employees would know of these interactions and the slow pace of remediation had left some with the incorrect perception that these issues had not been taken seriously. Otsuka Europe stated that it would enhance communication to employees around this issue and had implemented a series of weekly Town Hall style updates.

Otsuka Europe noted the complainants' concern that distribution lists for the communication of SPC and prescribing information revisions were not kept up-to-date. but noted that in that regard it had taken two important steps to address this issue.

In Case AUTH/3041/6/18, Otsuka Europe acknowledged that emails notifying affiliates of SPC or prescribing information changes had not reached their destinations due to poorly maintained mailing lists. The company standardized its process to use generic email inboxes in each affiliate, implementing them where they did not exist. This substituted for the named individuals and reduced the need to maintain the mailing list. Additionally, as previously explained in Case AUTH/3123/11/18, tracking the implementation of SPC/prescribing information revisions in each affiliate was a remediation Otsuka Europe took to address these communication issues.

Specifically, the first step in this tracking was an acknowledgement that the communication on changes to SPC and prescribing information had been received by the affiliate or third party; failure to respond in a very short timeframe would be noted and appropriate action taken. This check was put in place specifically after noting the failures in Cases AUTH/3041/6/18 and AUTH/3042/6/18; it ensured that communication was received by the affiliates and third parties, and thereby mitigated the risk that an email address change would be overlooked and not correctly added to the mailing list.

As the complainants noted, Otsuka Europe needed to continue to improve the process to remove incorrect

or outdated emails from the mailing list. In the new version of EU-SOP-MA-002, the mailing list would be simplified to remove all named individuals.

Otsuka Europe denied any breach of the Code with regard to this allegation.

**Confusion in relation to timelines**

Otsuka Europe noted the complainants' references to the timelines included in the communication of a prescribing information revision sent out on 21 December 2018. These timelines were calculated incorrectly and caused some affiliates to question the provided dates. Otsuka Europe acknowledged that the current version had caused some confusion in relation to timelines for implementation of the SPC updates. As noted above, EU-SOP-MA-002 was being revised. Whilst Otsuka Europe admitted breaches of the Code with regard to the overall process, it did not believe that an incorrectly calculated timeline was a breach of the Code.

**Concern about EU-SOP-MA-002 and 'blame culture**

Otsuka Europe noted that the complainants referred to EU-SOP-MA-002 being updated 'from scratch'. As noted above, the relevant SOP was being rewritten; there continued to be failings in the relevant process and the company was addressing that as a matter of urgency. Otsuka Europe acknowledged breaches in this regard as stated above.

In relation to the allegation of a 'blame culture' at Otsuka Europe, and a 'climate of fear' where employees expressed concerns about retaliation, it was important to recognize that individuals' perceptions were their realities. Otsuka Europe recognized that the very nature of these complaints indicated at least one or more employees had this concern about the company's culture.

Otsuka Europe noted that its whistleblowing policy and its incident response procedure both specifically stated that employees would be protected from retaliation. A SpeakUp programme was re-launched in 2017. Employees could elevate concerns to the SpeakUp line or website via their direct manager, or through authorized recipients in the organization. During 2018, the company discovered that due to a firewall misconfiguration, 6 contacts to the SpeakUp line were not routed correctly. When identified, the issue was fixed and incidents were promptly acted upon. Other reporting mechanisms were not affected.

There had been a significant increase in incidents reported in January/February 2019. In 2018, 47 incidents were raised internally, 19 were specifically related to Otsuka Europe; in 2019 there had been 27 incidents recorded, 21 of which were specifically related to Otsuka Europe. Each of these incidents had been recorded; each complainant had been contacted; and each was being investigated according to priority.

Otsuka Europe recognized that these concerns and individual perceptions required it to make concerted efforts to address its culture and in February the company had set up a team to address culture head on. The team would engage employees via surveys, the weekly Town Hall style meetings and other mechanisms to positively change culture.

With regard to the complainants' comment about why an employee had left the organisation, Otsuka Europe stated that it did not comment on management discussions with individual employees, consistent with privacy and employment law requirements.

Regardless of the accuracy of the complainants' claims, Otsuka Europe did not believe that cultural issues were breaches of the Code.

**Summary**

Otsuka Europe considered that the mistakes made in the revision of the Jinarc prescribing information were regrettable and it acknowledged breaches of Clauses 9.1 and 2 of the Code in that regard.

The company did not consider that any of the additional information provided by the complainants amounted to a breach of the Code apart from those acknowledged. Otsuka Europe stated that it was addressing the five priority remediations as soon as possible. In the meantime, it would continue to track the implementation of SPC revisions in all European affiliates.

**PANEL RULING**

The Panel noted that Otsuka Europe's headquarters were based in the UK. Otsuka Europe was a member of the ABPI and thus obliged to comply with the Code.

The Panel noted the complainants' allegation that a communication sent by Otsuka Europe dated 21 December 2018 in relation to a change in the Jinarc summary of product characteristics (SPC) in December 2018 included incorrect implementation dates and was confusing and included out-of-date Jinarc prescribing information. The complainants also alleged that there was no central repository for prescribing information and no process for its creation; the process for updating the prescribing information and SPC were not correct; and the email distribution list for SPC/prescribing information revisions was not up-to-date. In addition, the complainants made allegations about what was said by a senior member of the European medical team and about oversight by Otsuka's global teams.

The Panel noted Otsuka Europe's submission that the SPC update in question related to the addition of blisters in wallet cards with new Marketing Authorization Holder (MAH) numbers. The Panel noted that the communication in question, dated 21 December 2018, included several required affiliate actions including timelines for, *inter alia*, distribution of the updated SPC and package leaflet, withdrawal of previous SPC, package leaflet and promotional materials and update of non-promotional materials. The timeline for actions were given in both the number of business days and the completion date.

The Panel noted that there was some confusion in that the number of business days did not appear to correlate with the completion date. The Panel noted that when the dates were queried by an Otsuka UK employee, the response was that for the purpose of calculating working days for implementation dates taking into account the Christmas and New Year period; 24 and 31 December were considered as 'non-working' days in addition to the national public holidays (25, 26 December and 1 January). It was not clear if this was communicated to all of the original email recipients or just the individual who had queried it.

The Panel noted Otsuka Europe's submission that the timelines stipulated in the communication in question were calculated incorrectly and caused some affiliates to question the dates provided. The Panel considered, however, that the completion dates in the email in question appeared to be correct if 24 and 31 December and the public holidays were not considered to be working days. The Panel was concerned to note that these specific/additional 'non-working days' did not appear to be either covered in the relevant SOP or to be widely communicated and in the Panel's view this caused confusion. The Panel noted that further confusion was caused by a senior member of Otsuka Europe incorrectly referring to the communication in question as 'the Jinarc SmPC change regarding gout', which was not so.

The Panel had no information with regard to the dates of actual implementation performed by the recipients of the email in question. Otsuka Europe made no submission in this regard and there was no allegation on this point.

The Panel noted that although a completion date was given, the confusion around how the dates were calculated (with regard to business days) and the lack of clear communication in this regard caused confusion with regard to a critical process and meant that Otsuka Europe had failed to maintain high standards in this regard. A breach of Clause 9.1 was ruled.

The Panel did not consider that the email demonstrated that senior European leaders did not understand the process and no breach of Clause 9.1 was ruled in this regard.

With regard to the incorrect prescribing information included in the communication in question, the Panel noted Otsuka Europe's timeline of events; the SPC was revised in July 2018 to include an extension to the indication in Section 4.1 (CKD stage 4) and the addition of abdominal pain as a common side effect to section 4.8; the prescribing information was updated at the time to reflect these SPC changes. There was then a further SPC change regarding the addition of acute liver failure to sections 4.4 and 4.8 and these changes were included in the revised September 2018 prescribing information. In November 2018, the SPC was revised due to a change of marketing authorisation holder and was revised again in December 2018 to include the addition of wallet card blisters; however, both the November 2018 and December 2018 prescribing information omitted the previously added information regarding CKD stage 4, abdominal pain and acute liver failure.
The Panel noted the general principle that prescribing information (defined by Clause 4.2) must be up-to-date and must comply with Clauses 4.1 and 4.2 of the Code. The prescribing information must be consistent with the SPC for the medicine. The Panel noted Otsuka Europe's submission that, although certified and distributed to affiliates, neither the November 2018 nor the December 2018 prescribing information was used in external materials. The Panel was unclear with regard to what Jinarc promotional material, if any, was in circulation during November and December. Otsuka Europe made no submission in this regard. The Panel noted that the complaint concerned the internal distribution of the Jinarc prescribing information dated December 2018 as an attachment to the email dated 21 December 2018; the complainant made no reference to its use on materials. The Panel considered that it had no evidence before it in this case that incorrect or out-of-date prescribing information was actually used and considered that there was no allegation concerning its use on materials and in that regard, ruled no breach of Clause 4.1. The Panel noted that the use of incorrect Jinarc prescribing information on materials was the subject of another complaint (Case AUTH/3041/6/18).

Although it appeared to the Panel, from information provided by both parties, that the errors in the December 2018 prescribing information had been identified internally prior to the Authority's receipt of the complaint and remedial action taken, the Panel considered that Otsuka Europe had failed to maintain high standards by certifying and widely distributing incorrect prescribing information which omitted important safety information and a change to the licensed indication and which had the potential to be used in multiple affiliates. The Panel therefore ruled a breach of Clause 9.1.

The Panel noted the allegation that there was no central repository for storing up-to-date prescribing information, no standard process for the creation of prescribing information and the process for updating the prescribing information and SPC was not correct despite the latest SOP. The Panel noted Otsuka's submission that it was developing a repository and a process for authoring/updating prescribing information, however, this was not currently in place. The Panel was concerned that there appeared to be a general lack of oversight and guidance with regard to prescribing information creation and revision and noted the errors that had occurred in the November and December 2018 Jinarc prescribing information. The Panel considered that prescribing information was critical information required in all promotional materials and had the potential to impact patient safety.
The Panel noted that Otsuka acknowledged that the relevant SOP, SOP-MA-002, still needed to be improved in relation to both SPC and prescribing information updates. The Panel considered that the lack of a clear process for both the creation and revision of prescribing information and SPC updates meant that Otsuka Europe had failed to

maintain high standards and a breach of Clause 9.1 was ruled.

With regard to the allegation that the email distribution list for the communication of SPC and prescribing information revisions contained individuals who had left the company and mailing lists were not kept up-to-date, the Panel noted that the complainants had provided no evidence that individuals who should have received the communication in question had been omitted from the distribution list. The Panel noted Otsuka Europe's submission that it used generic email inboxes in each affiliate, and it intended to simplify the mailing list in its new version of the relevant SOP to remove all named individuals. In the Panel's view, that the email in question had been sent to individuals who had left the company was not in itself a breach of the Code so long as individuals who should have received it had done so. In the Panel's view, the complainants had not discharged their burden of proof to show that a breach of the Code had occurred in this regard and no breach of Clause 9.1 was ruled.

The Panel noted the complainants' allegations that a senior member of the Otsuka Europe medical team stated that the SOP for SPC and prescribing information updates (EU-SOP-MA-002) was flawed but was still approved and trained out in order to 'test the affiliates'; and that he/she stated that Otsuka Europe could use legal privilege to prevent the PMCPA receiving all the necessary information. The Panel noted Otsuka Europe's submission that its investigation into the alleged comments found no evidence that these statements were made. The Panel noted that, nonetheless, it appeared that there had been an acknowledgement at the meeting in question that the SOP required improvement. One interviewee recalled use of the word 'flawed'. Otsuka Europe acknowledged that the SOP required improvement. The Panel considered that this was a serious allegation; self-regulation relied upon, *inter alia*, full transparency from companies. The parties' accounts differed. It was difficult to determine where the truth lay. The Panel noted, however, that the complainants bore the burden of proof and considered, on balance, that the burden of proof had not been discharged and it therefore ruled no breach of Clause 9.1.

The Panel noted the complainants' allegations with regard to its Japanese parent company, global quality, regulatory and safety team, global medical and pharmacovigilance. The Panel noted Otsuka's submission that there had been consistent oversight, communication and provision of advice where considered appropriate from the above mentioned groups and that it refuted the allegation that Otsuka's global organisations had failed to take a more involved approach with respect to the issues related to the SPC implementation process. The Panel noted that rulings were made based on the evidence provided by both parties and that the complainants bore the burden of proof. The extent to which these allegations came within the scope of the Code in relation to global was unclear. Otsuka had made no submission on this point. The complainants had provided no detail with regard to this allegation and, in the Panel's view, the complainants had not discharged their burden of proof. No breach of

Clause 9.1 was ruled in this regard.

With regard to the allegation that there was a prevalent blame culture within the organisation and a climate of fear. The Panel considered that comments about the culture of an organisation might fall within the scope of the Code if that culture directly or indirectly contributed to a breach of the Code. The Panel noted Otsuka's submission that Otsuka Europe had a whistleblowing procedure and an incident response procedure which specifically stated that employees would be protected from retaliation. The complainants had provided no detail with regard to this allegation and, in the Panel's view, the complainants had not discharged their burden of proof. No breach of Clause 9.1 was ruled in this regard.

The Panel noted its comments and rulings above. The Panel noted that Clause 2 was a sign of particular censure and reserved for such use. On balance, the Panel did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 and ruled no breach accordingly. The complainants appealed this ruling.

**APPEAL BY THE COMPLAINANT**

The complainants appealed against the Panel's ruling of no breach of Clause 2.

The complainant's alleged that Otsuka had reduced confidence in the pharmaceutical industry for the following reasons:

- Unclear communication for the update of materials for new prescribing information – (a breach of Clause 9.1).
- Failed to maintain high standards by certifying and widely distributing incorrect prescribing information which omitted important safety information and a change to the licensed indication (breach of Clause 9.1).
- Unable to remediate a critical process (distribution of updated SPC and prescribing information) despite an initial PMCPA complaint in June 2018.

**RESPONSE TO APPEAL**

Otsuka Europe submitted that as acknowledged in its initial response, it had admitted to two breaches of Clause 2 due to:

- Otsuka Europe's inability to effectively remediate the issues highlighted in Case AUTH/3041/6/18 and the continued failure to address the issues.
- Not effectively achieving one of the key objectives of EU-SOP-MA-002 v6.0 'Notification of Changes to SPC, PL and prescribing information by OPEL/OPNL/ONPG to the OPEL affiliates and relevant Third Parties', to ensure that up-to-date information was provided when performing promotional activities via the prescribing information.

Thus, Otsuka Europe agreed with the complainants in this case that the cumulative effect of the issues reduced confidence in and brought the industry in to disrepute.
Whilst Otsuka Europe acknowledged the above, it considered it was vital that the Appeal Board understood the significant actions that had been taken in order to address these and other issues faced:

- Otsuka Europe confirmed that EU-SOP-MA-002 v6.0 the European process which included the creation and communication of prescribing information had been comprehensively reviewed and clarified and had been effective since 30 April 2019.
- Otsuka Europe submitted that as part of its response to Case AUTH/3151/1/19 it committed to reviewing all of the prescribing information and as a result of this review it submitted a voluntary admission (24 June 2019), detailing the outcome of the review including the identified discrepancies between the prescribing information and the relevant SPC. All prescribing information was comprehensive and fully consistent with the SPC. Although not a Code requirement Otsuka Europe had taken and implemented the decision to include all adverse events in the prescribing information in order to remove the element of subjectivity as to which adverse events should be included (in particular in relation to serious side effects), to avoid further issues in the future.
- Details of various staff changes and appointments were provided.
- As communicated to the PMCPA on 6 April 2019, Otsuka Europe had ceased initiating promotional and non-promotional activities unless such activities were required for legal, regulatory (eg, prescribing information and risk minimisation materials) or contractual reasons. The latter included work done jointly with Alliance partners. From June 2019, any Otsuka Europe signatories had to have completed comprehensive third party validation.
- A cross-functional project team had developed Otsuka Europe specific procedures for all Code-related activities conducted by Otsuka Europe, in order to provide the depth of detail required by the organisation. These had been extensively reviewed and were currently being cross-checked to ensure that they were robust. These would then be rolled out with comprehensive face-to-face training and knowledge and would then be validated via Otsuka's learning management system.
- The July meeting of the newly formed European Pharmaceutical Leadership Team (EPLT) included an assessment of the current challenges faced by Otsuka Europe, what the future held for the organisation and what the leadership team wanted, and how the leadership team intended to achieve their goals. Details were provided. These included:

    - Creation of a Vision and Roadmap to 2024.
    - Strategy to achieve Roadmap to 2024.
    - Continue to strengthen Culture & Engagement.
    - Continue CORE activities.
    - Get the 'Basics' right on business processes.

The above goals were presented at a town hall meeting in July 2019.

- A European Code of Conduct for all employees that would set out the ethical standards for employees to adhere to was being developed.
- Otsuka Europe was committed to transparent communication within the organisation and expected the same from its leadership team. In addition to the weekly town hall meetings, Otsuka Europe had instituted weekly 'Ask EPLT' sessions where any staff member might ask questions as part of a small group in a more informal setting.

Otsuka Europe hoped that the above demonstrated the approach that Otsuka Europe was taking to address the significant issues that it faced.

**FINAL COMMENTS FROM THE COMPLAINANT**

The complainants acknowledged that Otsuka Europe accepted a breach of Clause 2. However, the complainants were unclear as to why it had taken nearly eight months to review all associated prescribing information, especially as Otsuka Europe had committed to do so at the beginning of the year.

Could Otsuka claim to take patient safety seriously if the prescribing information did not have all the relevant safety information? What was the duration of the inconsistencies, and was the Pharmacovigilance/Global made aware of the risk to patient safety? If Pharmacovigilance/ Global was aware, what were their actions? The complainants did not understand the claim that the European process which included the creation and communication of prescribing information had been comprehensively reviewed and clarified and had been effective since 30 April 2019, if this was true, why was the voluntary submission made on 24 June 2019? Did this indicate that the process had failed, especially concerning the latest SPC change?

The complainants stated that Otsuka's current leadership needed more tangible outputs and they had not seen a significant difference between the past and present leadership.

**APPEAL BOARD RULING**

The Appeal Board noted from the Panel's rulings above that there was a lack of clear process for both the creation and revision of prescribing information and SPC updates; that Otsuka Europe had certified and internally distributed to multiple affiliates incorrect prescribing information which omitted important safety information and a change to the licensed indication; and that the lack of clear communication about completion dates for an SPC update caused confusion with regard to a critical process had meant that Otsuka Europe failed to maintain high standards and three separate breaches of Clause 9.1 were ruled.

The Appeal Board noted that Otsuka Europe agreed with the complainants' appeal that the cumulative effect of the issues warranted a breach of Clause 2. The company apologised for its inability to

effectively remediate the issues highlighted in Case AUTH/3041/6/18, and its continued failure to address the issues with regard to SPC updates and prescribing information. Otsuka Europe submitted that these failings had reduced confidence in the pharmaceutical industry. The Appeal Board was very concerned about how long it was taking Otsuka Europe to address these issues. The representatives from Otsuka Europe stated that this delay was due to the company failing to understand the role of prescribing information in relation to patient safety.

The Appeal Board considered that the cumulative effect of Otsuka Europe's failings in this case reduced confidence in the pharmaceutical industry and ruled a breach of Clause 2. The appeal on this point was successful.

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|---|---|
| **Complaint received** | **24 January 2019** |
| **Case completed** | **16 October 2019** |

**CASE AUTH/3153/1/19**

# ANONYMOUS v OTSUKA EUROPE

## Out-of-date promotional materials

**An anonymous, non-contactable individual who described themselves as a recent employee at Otsuka complained about material used at two overseas meetings. The complainant submitted that he/she had reported the matters at issue but as nothing had happened, decided to complain to the Authority.**

**The first matter concerned an alleged out-of-date advertisement that was used in association with a congress in France held in March 2018 (European Psychiatric Association (EPA)) which the complainant alleged was non-compliant.**

**Secondly, the complainant alleged that materials used at the European College of Neuropsychopharmacology (ECNP) Congress held in Spain in October 2018 were unapproved.**

**The detailed response from Otsuka Europe is given below.**

**The Panel noted Otsuka Europe's submission that it had made funding available for Otsuka France to support the EPA Congress and as part of its sponsorship agreement it could place an advertisement in the final congress programme. The advertisement used was retrieved from the CNS Resource Centre, for which it appeared Otsuka Europe was responsible.**

**The Panel ruled a breach, as acknowledged by Otsuka Europe, as the withdrawn advertisement placed in the EPA Congress programme had not been certified for such use.**

**The Panel considered that Otsuka Europe had failed to maintain high standards in relation to governance of withdrawn materials and a breach was ruled as acknowledged by Otsuka Europe.**

**Whilst the Panel was very concerned that withdrawn material was available in the CNS Resource Centre and that it appeared, from Otsuka Europe's submission, that there was only an informal agreement with the affiliates that if they used any material from the resource centre they must first obtain local approval for the item, it did not consider that the circumstances were such as to warrant a breach of Clause 2 which was a sign of particular censure. On balance, no breach of Clause 2 was ruled.**

**The Panel noted Otsuka Europe's submission that it had both promotional and non-promotional materials and activities at the ECNP Congress.**

**The Panel noted Otsuka Europe's submission that of the 64 job bags relating to pieces of material used at or in relation to the congress, 62 had one or more errors including not being certified, being certified incorrectly, being certified after first use and being used before the final hard copy was certified. According to interview notes materials included slides, invitations, agenda, abstract book and banner stand. The Panel therefore ruled a breach of the Code as acknowledged by Otsuka Europe.**

**The Panel noted Otsuka Europe's submission that its formal approval process in place at the time was not followed in relation to the certification and/or checking of material used at the congress. The Panel considered that Otsuka Europe had failed to maintain high standards and a breach was ruled.**

**The Panel noted the importance of certification and its role in underpinning the self-regulatory compliance system. The Panel noted the scale of errors. In addition, the Panel noted that these included a number of materials that had been used prior to final certification. In the Panel's view, the cumulative effect of the errors was that Otsuka Europe had reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.**

**The Panel did not consider that the complainant had provided evidence that compliance had attempted to cover up the issues or were not doing anything about them as alleged and therefore ruled no breach of the Code in this regard.**

An anonymous, non-contactable individual who described themselves as a recent employee at Otsuka complained about the promotional practices of Otsuka UK. The complaint was about material used at two overseas meetings. The complainant submitted that he/she had reported the matters at issue but as nothing had happened, decided to complain to the Authority.

**COMPLAINT**

The first matter concerned an alleged out-of-date advertisement that was used in association with a congress in the South of France held in March 2018 which the complainant alleged was non-compliant.

Secondly, the complainant alleged that materials used at the European College of Neuropsychopharmacology held in October 2018 were unapproved. The complainant stated that he/she had tried to chase an individual in medical but that he/she had refused to sign-off the materials. The complainant alleged that the compliance people were covering up the matter because the individual from medical was senior but that this was wrong.

When writing to Otsuka, the Authority asked it to bear in mind the requirements of Clauses 2, 7.2, 9.1, 14.1 and 14.2 of the 2016 Code.

**RESPONSE**

In a preliminary response Otsuka UK and Otsuka Europe noted that the two events referred to by the complainant were the European Psychiatric Association (EPA) Congress in Nice, France, 3-6 March 2018; and the European College of Neuropsychopharmacology (ECNP) Congress in Barcelona, Spain, 6-9 October 2018. Otsuka Pharmaceuticals Europe, not Otsuka UK had a presence at these meetings. No one from Otsuka UK attended the EPA and only one member of the Otsuka UK medical department attended the ECNP as a delegate; he/she was not involved in any Otsuka Europe activities at the conference (eg he/she did not staff the Otsuka Europe stand). Otsuka UK was not involved in any of the planning for these meetings or the production/sign off of any of the associated materials including the material provided by the complainant.

Both Otsuka Europe and Otsuka UK were one company (Otsuka) and were committed to self-regulation and high ethical standards. However, given Otsuka UK had no role in either congress at issue or in the approval of any material used at those meetings, Otsuka Europe asked if only it could respond to the case.

In its subsequent response, Otsuka Europe reiterated that the two events cited by the complainant, the EPA Congress and the ECNP Congress, were its responsibility.

The EPA congress took place in Nice from 2-6 March 2018. Otsuka Europe stated that it did not provide any support directly for the meeting, however, it made available funding to the affiliates should any wish to support the congress. Otsuka France decided to sponsor the congress, but Otsuka Europe submitted that it was responsible for the sponsorship as it had provided the funding for the congress. Otsuka UK had no role in the congress.

Otsuka France put in place a sponsorship agreement with the EPA which stated that, in return for funds, Otsuka France would be a Gold Sponsor of the event and Otsuka France cross-charged Otsuka Europe for the cost of sponsoring the congress. Part of this package was that Otsuka France could place an advertisement in the final programme (a copy of the sponsorship contract was provided).

Otsuka Europe did not have any presence at the meeting other than three employees who attended as delegates. After returning from the congress, one of the Otsuka Europe attendees realised that there was an Abilify Maintena advertisement on what was described as the conference abstract book (the final programme) that contained several mistakes; this was raised internally at Otsuka Europe as an incident on 7 March 2018.

Otsuka Europe explained that at the end of January 2018, an employee who had recently joined Otsuka France emailed an employee at Otsuka Europe to ask for an advertisement in English for Abilify Maintena and the contact details for a particular employee from the UK. The Otsuka Europe employee directed his/her Otsuka France colleague to the 'CNS Resource Centre'; this was a resource for the affiliates that provided access to marketing materials for Otsuka CNS products; it was also an archive of previously used material. As part of this email conversation, the European employee also, by way of introduction, copied in a UK employee.

The Otsuka France employee retrieved the advertisement in question from the CNS Resource Centre and suggested in the email conversation that this was used. The UK employee stated that the advertisement had already been withdrawn and the European employee directed his/her French colleague to other materials in the CNS Resource Centre and attached a current example.

The French employee initially sent the out-of-date advertisement on to the agency in charge of the congress, but then sent the replacement advertisement stating 'Can you please use this Ad instead of the first one I sent you?'. An email from the agency received by the employee when he/she submitted the final advertisement indicated that it had been accepted. However, the advertisement which was placed in the final programme was not the replacement version sent by the Otsuka France employee. Only after the event when questions were asked of the agency was Otsuka France told that it had missed the deadline for submission for changes to the printed material.

The advertisement placed in the final programme had in fact been withdrawn from the approval system in March 2017 but remained as a resource for the affiliates as the resource centre was also an archive. The informal agreement with the affiliates was that if they used any material from the resource centre, they must first obtain local approval for the item. Unfortunately, Otsuka France sent the advertisement at issue to EPA without local approval. This was the advertisement that was used on the EPA booklet, a partial copy of which was provided to the PMCPA by the complainant. A copy of the full advertisement certified by Otsuka Europe in 2014 was provided.

As a result of the above, the CNS Resource Centre was closed in March 2018 and relaunched in June 2018 with current material only. In addition, every item had a watermark which stated that local approval was required before the affiliates could use it.

As well as lacking prescribing information, the advertisement had not been certified since the initial certification on 9 January 2014 and referred to Abilify Maintena as 'new'. Otsuka Europe acknowledged that as the material was used in 2018 there had been a failure to recertify material that was still in use beyond the two years post-certification; the relevant clause was Clause 14.5 however, the company noted that it had not been asked to consider the requirements of that clause. Nevertheless, it considered that continued use without recertification amounted to a breach of Clause 14.1.

In relation to the use of 'new' in the advertisement beyond the permitted 12 months after the

medicine was generally available, Otsuka Europe acknowledged a breach of Clause 7.11. Again, the company had not been asked to respond in relation to the requirements of that clause, but rather Clause 7.2; Otsuka Europe considered that the use of 'new' in relation to the medicine was misleading, in breach of Clause 7.2.

The advertisement printed in the congress booklet did not contain prescribing information, contrary to the requirements as it was certified by a UK company (Otsuka Europe) and therefore prescribing information was required to be provided and so Otsuka Europe acknowledged a breach of Clause 4.1, although it noted that it had not been asked to consider the requirements of that clause.

Otsuka Europe acknowledged that maintaining material that had been withdrawn in a central repository, without making it abundantly clear that the item required additional approval before use, amounted to a failure to maintain high standards and had the potential to bring the industry into disrepute, in breach of Clauses 9.1 and 2.

Otsuka Europe did not consider that Clause 14.2 was relevant in relation to the EPA, given that the company did not take any health professionals to the congress or support their attendance in any way.

The European College of Neuropsychopharmacology (ECNP) Congress took place in Barcelona, from 6-9 October 2018. This was a major conference for Otsuka in 2018 and Otsuka Europe had both promotional and non-promotional materials and activities at the congress, for example, symposia and meetings led by medical, a promotional booth, a medical information booth and other material.

There was an internal incident raised on 12 December 2018 that there were a number of items used at the congress without being formally approved in the electronic approval system. This was logged in the incident registry and an investigation launched. There were two other similar incidents raised and logged in January 2019. Otsuka Europe stated that it did not have an explanation for the delay in the incident being reported; however, face-to-face training on its revised standard operating procedure (SOP) for promotional and non-promotional material approval had been conducted on 23 and 30 November, and on 3 December 2019.

Otsuka Europe explained that more than 60 pieces of material were used at or in relation to the congress. The internal incidents raised were in relation to medical-led materials and activities that were not certified and/or checked (in relation to printed items) before they were used at the congress. A relevant employee in medical left Otsuka shortly after the congress in October 2018; however, the company had spoken to members of staff who were involved in the preparation for the ECNP congress and/or who attended and certain relevant emails had been reviewed. Relevant staff in medical had been trained on the process.

There was extensive activity on email in relation to the approval of material for the congress. This was not surprising given that both Otsuka medicines in this therapy area were jointly promoted with a partner company that did not share the same electronic approval system as Otsuka Europe. During this time, there was a lengthy discussion as to whether the material should be classified as promotional or non-promotional.

Some months before the congress, most of the job bags relating to the planned material were created on the electronic approval system, but in some cases material was not progressed through the formal approval process until the first day of the congress, during the congress or after the congress had finished. Some staff were aware during the congress that material had not been approved or checked and attempted to address this, for example by asking signatories to certify material in Zinc whilst on site at the congress, or by taking photographs of hard copy material in order for a signatory to conduct a check of hard copy material. The review of material identified numerous procedural errors and issues.

Of the 64 job bags, 62 had one or more errors. Otsuka Europe acknowledged that the formal approval process in place at the time was not followed in relation to the certification and/or checking of material used at the congress. Additionally, materials were not certified in time for use at the congress, the gallery notes did not always support the certification being an attestation that the material would have been approvable and was not always clear it was not a retrospective approval. Additionally, a large number of the certification errors appeared after the employees who made them attended a series of face-to-face baseline trainings on the Code, including approval standards.

Given that certain material was not certified, or checked where required, before use, Otsuka Europe accepted a breach of Clause 14.1. It appeared that internal process was not followed for a large number of items that were used at the congress, and the company acknowledged that this amounted to a failure to maintain high standards, in breach of Clause 9.1. The company also considered that such poor planning in approach for a congress where Otsuka had a major presence brought the industry into disrepute, in breach of Clause 2.

Otsuka Europe noted the complainant's comment that 'I don't think that the compliance people are doing anything except covering this up'. As noted above, Otsuka Europe had a process for handling internal incident reports. The issues raised by the complainant had both been raised internally with the European compliance department and were logged on the incident register when they were reported and the individual raising the concern was so informed. In the case of the EPA congress, the incident was investigated and closed out in October 2018. In the case of the ECNP, the investigation was ongoing when this complaint was received.

Given the concern raised by the complainant in this case that compliance was 'covering up' these

incidents, European compliance requested an internal investigation in to how these incidents were processed. A copy of the report from this investigation was provided. The report concluded that the concerns raised were handled appropriately. Given this, Otsuka Europe did not consider that there has been any breach of the Code in this regard.

Otsuka Europe stated that on the evening of 13 February 2019, a senior employee received a self-identified report that five items used at a third congress, the European Haematology Association, held from 14-17 June 2018 in Stockholm, Sweden, were approved but not certified before use. The five items included ones that both would and would not be required to be certified under the Code. An incident was raised and an investigation was pending; there was not enough time to conduct a thorough review before submitting this response. Therefore, given the information it currently had on hand, Otsuka Europe considered this was a breach of Clause 14.1. Additionally, given the fact that the pattern repeated across two Otsuka Europe-led events, the company considered this a failure to maintain high standards and therefore a breach of Clause 9.1. If the investigation provided any different conclusions on root causes than those identified as part of the investigation into ECNP, Otsuka Europe would provide a summary to the PMCPA including an evaluation of the applicability of Clause 2, as well as an amended remediation plan.

In response to these serious and repeated failures to ensure material was properly reviewed and certified before use, and that certified material complied with the Code, Otsuka Europe would complete a review of all current materials which it still used in 2018, starting with all currently effective materials. This would be completed by May 2019. Additionally, it had already started a review of the currently planned congresses for 2019, which would complete by 31 March 2019. Finally, all employees with a role in the planning, execution, or approval of congresses would be retrained by May 2019 and the company planned comprehensive retraining and validation of all signatories.

**PANEL RULING**

The Panel noted Otsuka's submission that Otsuka Pharmaceuticals Europe, not Otsuka UK had a presence at the two meetings referred to by the complainant. The Panel noted that Otsuka Europe was based in the UK and was a member of the ABPI and, as such, it was obliged to comply with the Code. Otsuka Europe had responded to the complaint.

In the Panel's view, Otsuka Europe would not necessarily be held responsible for the activities of its affiliates if its only role was to be cross-charged by the affiliate for the activity in question. Whether Otsuka Europe was responsible, and whether the Code applied, would be determined on a case-by-case basis taking into account all the circumstances including: Otsuka Europe's role in relation to the activity and whether such activity was directed or encouraged by Otsuka Europe.

**European Psychiatric Association (EPA) Congress**

The Panel noted Otsuka Europe's submission that it had made funding available for Otsuka France to support the EPA Congress. In the Panel's view, the proactive offering of funding to its affiliate for a specific meeting meant that Otsuka Europe had some responsibility with regard to the sponsorship. The Panel noted Otsuka Europe's submission that it was responsible for the sponsorship of the EPA Congress.

The Panel noted that Otsuka France as part of its sponsorship agreement with the EPA could place an advertisement in the final congress programme. The Panel noted that the advertisement placed in the final congress programme was retrieved by a recently appointed Otsuka France employee from the CNS Resource Centre, for which it appeared Otsuka Europe was responsible, after being directed to it by a European employee. The Panel noted Otsuka Europe's submission above about how the advertisement in question, which was withdrawn in March 2017, came to be published.

The Panel noted its comments above with regard to Otsuka Europe and its responsibility for the sponsorship of the EPA Congress. The Panel further noted Otsuka Europe's responsibility with regard to the 'CNS resource centre' to which the Otsuka France employee was directed by an Otsuka Europe employee. In the Panel's view, the advertisement in the Congress programme fell within the scope of the UK Code; Codes, laws and regulations in other countries might also be applicable. The Panel noted that it could only make rulings with regard to the UK Code.

The Panel noted the narrow allegation; that the advertisement in question was out of date which the complainant considered to be non-compliant. The complainant made no allegation about the content of the advertisement. The Panel considered that there was no allegation in relation to Clause 7.2 and 14.2 as cited by the case preparation manager and thus the Panel made no ruling in relation to these clauses. In addition, the Panel noted that Otsuka Europe had unilaterally raised and responded to Clauses 4.1 and 7.11 which were not the subject of complaint and thus the Panel made no ruling on these clauses.

The Panel noted that the withdrawn advertisement had been placed in the EPA Congress programme and had not been certified for such use. The Panel therefore ruled a breach of Clause 14.1 as acknowledged by Otsuka Europe.

The Panel noted Otsuka Europe's submission that maintaining material that had been withdrawn in a central repository, without making it abundantly clear that the item required review and approval before use, amounted to a failure to maintain high standards. The Panel further noted that an Otsuka Europe employee had directed an Otsuka France employee to the resource centre.

The Panel considered that Otsuka Europe had failed to maintain high standards in relation to governance

of withdrawn materials and a breach of Clause 9.1 was ruled as acknowledged by Otsuka Europe. The Panel noted its rulings and comments above. Whilst the Panel was very concerned that withdrawn material was available in the CNS resource centre and that it appeared, from Otsuka Europe's submission, that there was only an informal agreement with the affiliates that if they used any material from the resource centre they must first obtain local approval for the item, it did not consider that the circumstances were such as to warrant a breach of Clause 2 which was a sign of particular censure. On balance, no breach of Clause 2 was ruled.

**European College of Neuropsychopharmacology (ECNP) Congress**

The Panel noted Otsuka Europe's submission that it had both promotional and non-promotional materials and activities at the ECNP Congress which took place in Barcelona, from 6-9 October 2018, for example, symposia and meetings led by medical, a promotional booth, a medical information booth and other materials. The Panel noted that Otsuka Europe had responsibility under the UK Code as the organiser of these materials and activities. Codes, laws and regulations in other countries might also be applicable. The Panel noted that it could only make rulings with regards to the UK Code.

The Panel noted Otsuka Europe's submission that of the 64 job bags relating to pieces of material used at or in relation to the congress, 62 had one or more errors including not being certified, being certified incorrectly, being certified after first use and being used before the final hard copy was certified. According to interview notes materials included slides, invitations, agenda, abstract book and banner stand. The Panel therefore ruled a breach of Clause 14.1 as acknowledged by Otsuka Europe.

The Panel noted that Clause 14.2 of the 2016 Code required all meetings involving travel outside the UK where a UK company funded delegates to be certified in advance. In addition, all meetings involving travel outside the UK that were wholly or mainly for UK delegates must also be certified in advance. The Panel noted that neither of these appeared to be the case with regards to the ECNP Congress and therefore, in the Panel's view, Clause 14.2 was not relevant and it made no ruling in that regard.

The Panel noted Otsuka Europe's submission that its formal approval process in place at the time was not followed in relation to the certification and/or checking of material used at the congress. The Panel considered that Otsuka Europe had failed to maintain high standards and a breach of Clause 9.1 was ruled. The Panel noted the importance of certification and its role in underpinning the self-regulatory compliance system. The Panel noted the scale of errors; of 64 job bags 62 had one or more errors. In addition, the Panel noted that these included a number of materials that had been used prior to final certification. In the Panel's view, the cumulative effect of the errors was that Otsuka Europe had reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

**Compliance**

The Panel noted Otsuka Europe's submission that it had a process for handling internal incident reports. The issues raised by the complainant had both been raised internally with the European compliance department and were logged on the incident register when they were reported and the individual raising the concern was so informed. In the case of the EPA congress, the incident was investigated and closed out in October 2018. In the case of the ECNP, the investigation was ongoing when this complaint was received.

The Panel noted Otsuka Europe's submission that given the complainant stated that compliance was 'covering up' these incidents, European compliance requested an internal investigation in to how these incidents were processed. The Panel noted that the report provided suggested that the concerns raised had been or were being handled appropriately.

The Panel did not consider that the complainant had provided evidence that compliance had attempted to cover up the issues or were not doing anything about them as alleged. The Panel therefore ruled no breach of Clause 9.1.

The Panel noted Otsuka Europe's submission that on 13 February 2019, a senior employee received a self-identified report that five items used at a third congress, the European Haematology Association, held from 14-17 June 2018 in Stockholm, Sweden, were approved but not certified before use and it considered this was a breach of Clause 14.1. The Panel noted Otsuka Europe's submission that the five materials included both those that would and would not require certification under the Code. The Panel noted that this matter had not been raised by the complainant and therefore it could make no ruling.

**Complaint received** **30 January 2019**

**Case completed** **5 July 2019**

Case AUTH/3154/2/19

# COMPLAINANT v DR FALK PHARMA

## Provision of obligatory information on a website

**An individual who described him/herself as a 'concerned UK health professional', complained about the Dr Falk Pharma website for health professionals and links from that website. The complainant referred to information provided for Budenofalk (budesonide, used to treat, *inter alia*, Crohn's disease), Salofalk (mesalazine, used to treat ulcerative colitis), Ursofalk (ursodeoxycholic acid, used to treat, *inter alia*, primary biliary cirrhosis) and Jorveza (budesonide, used to treat eosinophilic esophagitis).**

**The complainant noted that on the webpages for Budenofalk, Salofalk and Ursofalk, there was only a link to the relevant summary of product characteristics (SPC) and no prescribing information. In a media link there was a first mention of Jorveza but there was no generic name stated nor any link to prescribing information. An article on Jorveza, accessed by a link on the website, similarly had no prescribing information. A link to a different website took the reader to an advertisement for Budenofalk which included out-of-date prescribing information as two updates, which included details of special warnings, had not been included. Finally, a link to another published article had no prescribing information and it was not evident that the article was promotional although it was from a promotional website.**

**The detailed response from Dr Falk Pharma is given below.**

**The Panel noted that the complainant had only provided a screen shot of one part of the website and not shots of the other pages. Dr Falk Pharma had not been able to supply full details. In the Panel's view, it was important that complainants provided screen shots at the time of their complaint to ensure that the PMCPA had access to the same material as they did. A website could be updated by a pharmaceutical company immediately after the complainant viewed it and before the PMCPA had been notified.**

**The Panel noted from Dr Falk Pharma that the health professional section of the website was intended for registered health professionals only and was password protected. The media page and other pages were not password protected. The media page was intended for the press and media agencies. Dr Falk Pharma submitted that the article on Jorveza was available to readers once they clicked on the title of the article and that the link to the SPC including the prescribing information was also available.**

**The Panel noted that it appeared that the media pages on the website referred to the latest articles, press releases etc, content produced and published by Dr Falk Pharma for the media. In addition the media pages also appeared to include content where Dr Falk Pharma and/or its products were mentioned. This was described as 'Dr Falk Pharma in the media'. The Panel noted that on the pages for health professionals although there were links to the SPCs for (Budenofalk, Salofalk, and Ursofalk), prescribing information had not been provided. The links to the SPCs were not sufficient to meet the requirements of the Code. The legal classification and the cost were also required. The Panel therefore ruled breaches of the Code in relation to Budenofalk, Salofalk and Ursofalk.**

**In relation to the media link and the first mention of Jorveza, the Panel did not have access to the relevant material. Such a link should not be advertising and therefore although it might be helpful to give the non-proprietary name, there was no requirement to do so. Nor was there a requirement to include prescribing information. The Panel did not consider that the complainant had shown on the balance of probabilities that this material was promotional. Given the circumstances, the Panel ruled no breach of the Code.**

**In relation to the Jorveza article and the alleged lack of prescribing information, again the Panel noted that it did not have access as to how this appeared on the website. It appeared that the material was an article published in Pharmacy Magazine. The material provided by Dr Falk Pharma was headed 'New drug for eosinophilic oesophagitis' followed by a photograph of a woman who was clutching her stomach. The text below the photograph referred to Jorveza and its indication. The Panel considered that the material was in effect an advertisement for Jorveza. The prescribing information was not provided as part of the material but according to Dr Falk Pharma, a link to the SPC including the prescribing information was provided on the media page. The Panel noted that the media page link stated 'for more information about Jorveza please click here'. There was no mention that this was the link to the prescribing information and as there was no clear link a breach was ruled.**

**The Panel noted that the complainant had accessed a link from the Dr Falk Pharma website to an advertisement for Budenofalk which appeared in an online journal. The complainant provided the address for the link. The Panel had no information about the link from Dr Falk Pharma or from its website. Historical advertisements would be available in third party publications. If Dr Falk Pharma had provided a direct link to the historical advertisement then this was in effect the same as the company having that advertisement on its own website. The prescribing information in the advertisement for Budenofalk in Gastroenterology Today, Summer 2017 was not up-to-date at the time such a link was used. Given that the complainant**

**had provided the direct link and that the Dr Falk Pharma media page included links to Dr Falk Pharma in the media, the Panel decided, on the evidence before it, on the balance of probabilities, that the link was to the actual advertisement. Thus the Panel ruled a breach of the Code.**

**The Panel noted that the published article referred to by the complainant was a review of ursodeoxycholic acid in primary biliary cholangitis. If Dr Falk Pharma had a role in the production/publication of the article then this was not clear. The final page stated the author's conflict of interest as having served on advisory boards and lectured on behalf of Dr Falk Pharma and another company. The Panel did not consider it had sufficient information to understand the arrangements for the publication of the article. Having a published paper on a pharmaceutical company website was not necessarily promotional. The Panel did not consider that the complainant had shown, on the balance of probabilities, that this material was promotional and thus required prescribing information or that placing the article on the website amounted to disguised promotion as alleged. No breach of the Code was ruled.**
**The Panel noted its rulings set out above and ruled a breach as overall high standards had not been maintained. It did not consider the circumstances warranted a ruling of a breach of Clause 2 of the Code which was used a sign of particular censure.**

An individual who described him/herself as a 'concerned UK health professional', complained about the Dr Falk Pharma website for health professionals and links from that website. The complainant referred to information provided for all of Dr Falk Pharma's medicines ie Budenofalk (budesonide, used to treat, *inter alia*, Crohn's disease), Salofalk (mesalazine, used to treat ulcerative colitis), Ursofalk (ursodeoxycholic acid, used to treat, *inter alia*, primary biliary cirrhosis) and Jorveza (budesonide, used to treat eosinophilic esophagitis).

**COMPLAINT**

The complainant referred to five items. Firstly, the complainant noted that on the separate product pages for Budenofalk, Salofalk and Ursofalk, there was only a link to the relevant summary of product characteristics (SPC) and no prescribing information. Secondly, in a media link there was a first mention of Jorveza but there was no generic name stated nor any link to prescribing information. Thirdly, an article on Jorveza, accessed by a link on the website, similarly had no prescribing information. Fourthly, the complainant noted that a link to a different website (issuu.com) took the reader to an advertisement for Budenofalk which included out-of-date prescribing information as two updates, which included details of special warnings, had not been included. Finally, a link to another published article had no prescribing information and it was not evident that the article was promotional although it was from a promotional website.

When writing to Dr Falk Pharma, the Authority asked it to consider the requirements of Clauses 2, 4.1, 4.3, 9.1 and 12.1 of the 2016 Code.

**RESPONSE**

Dr Falk Pharma stated that it recognised the accidental omission of the prescribing information from its website and that it was working to remedy the matter; the prescribing information would be on the webpages shortly. The company had also reviewed the website in light of this complaint and was in the process of revising the content.

With regard to the out-of-date prescribing information, (the fourth allegation) Dr Falk Pharma noted that the complainant had referred to an advertisement for Budenofalk that appeared in the online version of Gastroenterology Today, Summer 2017. The prescribing information was dated October 2016 and related to the summaries of product characteristics (SPCs) dated July 2016 (granules) and November 2016 (capsules). The capsules SPC was updated after that of the granules and to come into line with the granules. The prescribing information and SPC were therefore correct when the advertisement was published. The SPC was not updated again until after publication. Dr Falk Pharma submitted that one of its standard operating procedures (SOPs) described the process to ensure the prescribing information was updated following revisions to the SPC. Current advertisements had the current prescribing information.

Dr Falk Pharma provided information on how its website was navigated.

In response to a request for further information, Dr Falk Pharma stated that the company was unable to provide a copy of the relevant media webpage as it had been updated and a copy was not kept. Copies of the article on Jorveza and the published article were provided. These were published on the media page of the website.

**PANEL RULING**

The Panel noted that the complainant had provided a screen shot of one part of the website. The complainant had not provided screen shots of the other pages. Dr Falk Pharma had not been able to supply full details. In the Panel's view, it was important that complainants provided screen shots at the time of their complaint to ensure that the PMCPA had access to the same material as the complainant. A website could be updated by a pharmaceutical company immediately after the complainant viewed it and before the PMCPA had been notified.

The Panel noted the information from Dr Falk Pharma about its website. The information was a presentation dated February 2019 and stated that the health professional section of the website was intended for registered health professionals only and was password protected. The media page and other pages were not password protected. The media page was intended for the press and media agencies. Dr Falk Pharma submitted that the article on Jorveza was available to readers once they clicked on the title of the article and that the link to the SPC including the prescribing information was also available here.

The Panel noted that it appeared that the media pages on the website referred to the latest articles, press releases etc, content produced and published by Dr Falk Pharma for the media. In addition the media pages also appeared to include content where Dr Falk Pharma and/or its products were mentioned. This was described as 'Dr Falk Pharma in the media'.

In relation to the list of products referred to by the complainant, (Budenofalk, Salofalk, and Ursofalk) the Panel noted that these appeared on the pages for health professionals and although there were links to the relevant SPCs on the Dr Falk Pharma website, prescribing information had not been provided. The links to the SPCs were not sufficient to meet the requirements in Clause 4.2 of the Code. This clause listed a number of elements which made up the prescribing information as required by Clause 4.1 and although many of these would be satisfied by the provision of the SPC, the legal classification and the cost were also required. The Panel therefore ruled breaches of Clause 4.1 of the Code in relation to Budenofalk, Salofalk and Ursofalk.

In relation the media link and the first mention of Jorveza, the Panel did not have access to the relevant material. Such a link should not be advertising and therefore although it might be helpful to give the non-proprietary name, there was no requirement to do so. Nor was there a requirement to include prescribing information. The Panel did not consider that the complainant had shown on the balance of probabilities that this material was promotional. Given the circumstances, the Panel ruled no breach of Clauses 4.1 and 4.3 of the Code.

In relation to the Jorveza article and the alleged lack of prescribing information, again the Panel noted that it did not have access as to how this appeared on the website. The presentation provided by Dr Falk Pharma gave some information. It appeared that the material was an article published in Pharmacy Magazine. The material provided by Dr Falk Pharma was headed 'New drug for eosinophilic oesophagitis' followed by a photograph of a woman who was clutching her stomach. The text below the photograph referred to Jorveza and its indication. The Panel considered that the material was in effect an advertisement for Jorveza. The prescribing information was not provided as part of the material but according to Dr Falk Pharma, a link to the SPC including the prescribing information was provided on the media page. The Panel noted that the media page link stated 'for more information about Jorveza please click here'. There was no mention that this was the link to the prescribing information. The Panel considered that there was no clear link to the prescribing information and a breach of Clause 4.1 was ruled.

The Panel noted that the complainant had accessed a link from the Dr Falk Pharma website to an advertisement for Budenofalk which appeared in an online journal. The complainant provided the address for the link. The Panel had no information about the link from Dr Falk Pharma or from its website. It was not clear whether it was a link to the actual advertisement or to the journal and then readers came across the advertisement. The Panel accepted that historical advertisements would be available in third party publications. If Dr Falk Pharma had provided a direct link to the historical advertisement then this was in effect the same as the company having that advertisement on its own website. The prescribing information in the advertisement for Budenofalk in Gastroenterology Today, Summer 2017 was not up-to-date at the time such a link was used. This would be a breach of Clause 4.1 of the Code. Given that the complainant had provided the direct link and that the Dr Falk Pharma media page included links to Dr Falk Pharma in the media, the Panel decided, on the evidence before it on the balance of probabilities, that the link was to the actual advertisement. Thus the Panel ruled a breach of Clause 4.1.

The Panel noted that the published article referred to by the complainant was a review of ursodeoxycholic acid in primary biliary cholangitis. If Dr Falk Pharma had a role in the production/publication of the article then this was not clear. The final page stated the author's conflict of interest as having served on advisory boards and lectured on behalf of Dr Falk Pharma and another named company. The Panel did not consider it had sufficient information to understand the arrangements for the publication of the article. Having a published paper on a pharmaceutical company website was not necessarily promotional. For example, the supplementary information to Clause 26.2 referred to reference information made available for medicines with marketing authorisations and that this could include published papers. The Panel did not consider that the complainant had shown, on the balance of probabilities, that this material was promotional and thus required prescribing information. The Panel therefore ruled no breach of Clause 4.1 of the Code. The Panel did not consider that placing the article on the website amounted to disguised promotion as alleged and thus ruled no breach of Clause 12.1 of the Code.

The Panel noted its rulings set out above and considered that overall high standards had not been maintained with the website. The Panel therefore ruled a breach of Clause 9.1 of the Code. It did not consider the circumstances warranted a ruling of a breach of Clause 2 of the Code which was used a sign of particular censure.

**Complaint received** **4 February 2019**

**Case completed** **24 May 2019**

# COMPLAINANT v BRISTOL-MYERS SQUIBB AND PFIZER

## Eliquis website

**A complainant who described him/herself as a 'concerned UK health professional' complained about the Eliquis (apixaban) website. Eliquis, co-marketed by Bristol-Myers Squibb and Pfizer, was an antithrombotic.**

**The complainant noted that pages of the Eliquis website which detailed special warnings and precautions for use, stated that care was to be taken if patients were treated concomitantly with non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin. That statement, however, differed significantly with the latest version of the summary of product characteristics (SPC) which stated that care was to be taken if patients were treated concomitantly with selective serotonin re-uptake inhibitors (SSRIs) or serotonin norepinephrine re-uptake inhibitors (SNRIs), or NSAIDs, including acetylsalicylic acid (aspirin). The complainant submitted that this could potentially be a patient safety issue.**

**The detailed response from Bristol-Myers Squibb and Pfizer is given below.**

**The Panel noted that the website in question was for health professionals and was headed 'Practical Information To assist your daily practice'. The section giving guidance on special warnings and precautions for use referred to a number of factors to consider; including 'interaction with other medicinal products affecting haemostasis'. The information in this part of the website included the need to take care if patients were treated concomitantly with NSAIDs including aspirin and concluded that 'Further information on interactions with other medicinal products is available in the Eliquis SmPC'. The template for the website included links to the prescribing information, the adverse event reporting information, the SPC and to the patient information leaflet. At the end of the list of factors to consider was a reference to 'see Eliquis SmPC for full prescribing information'.**

**The Panel noted the Alliance's submission that the links provided were to the amended SPC and prescribing information which had the information that care was to be taken if patients were treated concomitantly with SSRIs or SNRIs or NSAIDs including acetylsalicylic acid (Section 4.4) and that Eliquis should be used with caution when coadministered with SSRIs, SNRIs or NSAIDs (including acetylsalicylic acid) because these products typically increased the bleeding risk (Section 4.5).**

**The Panel considered that only referring to the cautions for coadministering NSAIDs and not referring to similar cautions with SSRIs or SNRIs on a detailed page about special warnings and precautions for use was misleading. The Panel ruled a breach of the Code. The Panel considered that although misleading, the omission did not necessarily mean that the material was inconsistent with the SPC and therefore ruled no breach of the Code.**

**The Panel ruled that the companies had failed to maintain high standards in breach of the Code.**

**The Panel noted its comments above and that neither SSRIs nor SNRIs were contra- indicated with Eliquis and health professionals would be cautious when initiating any therapy. The Panel considered that in the particular circumstances of this case the omission of information about the need for care if SSRIs or SNRIs were coadministered with Eliquis did not warrant a ruling of a breach of Clause 2 which was reserved as a sign of particular censure.**

A complainant who described him/herself as a 'concerned UK health professional' complained about the Eliquis (apixaban) website. Eliquis, co-marketed by Bristol-Myers Squibb and Pfizer, was an antithrombotic.

**COMPLAINT**

The complainant noted that pages of the Eliquis website which detailed special warnings and precautions for use, stated that care was to be taken if patients were treated concomitantly with non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin. That statement, however, differed significantly with the latest version of the summary of product characteristics (SPC) which stated that care was to be taken if patients were treated concomitantly with selective serotonin re-uptake inhibitors (SSRIs) or serotonin norepinephrine re-uptake inhibitors (SNRIs), or NSAIDs, including acetylsalicylic acid (aspirin). The complainant submitted that this could potentially be a patient safety issue.

When writing to advise Bristol-Myers Squibb and Pfizer of the complaint, the Authority asked both companies to consider the requirements of Clauses 2, 3.2, 7.2 and 9.1 of the 2016 Code.

**RESPONSE**

Bristol-Myers Squibb responded on behalf of both companies (the Alliance) and stated that the special warnings and precautions for use section of the Eliquis website was approved and went live in May 2018 (webpage job number 432UK1800403-06).

The Alliance explained that the Eliquis SPC received a positive Committee for Medicinal Products for Human Use (CHMP) opinion on 18 June 2018 (date

of revised SPC) to include additional information regarding SSRIs and SNRIs in Sections 4.4 and 4.5. On receipt of the European Commission Decision on 3 August 2018, the final SPC of Eliquis was made available for UK health professionals as was the prescribing information and revised Eliquis materials.

In accordance with the relevant company standard operating procedures (SOPs) both companies prepared a list of all valid Eliquis promotional materials in use including the Eliquis website to ensure the review and re-approval in light of the SPC update. The majority of the materials only required the inclusion of updated prescribing information and/or SPC and no content revision was needed.

The Eliquis webpage in question was reviewed, and the links to the updated SPC/prescribing information were included. The content on the webpage included interactions with other medicines which affected haemostasis. A clear statement in the section stated, 'Further information on interactions with other medicinal products is available in the Eliquis SPC' and the latest SPC/prescribing information were directly linked on this page. However, in hindsight, the content in this particular webpage would have benefitted from being revised to additionally include the information related to SSRIs and SNRIs. The Alliance appreciated that this might have caused confusion and ambiguity to the readers and therefore it was being updated.

With regard to Clause 7.2, the Alliance submitted that all the information provided was accurate and fair in its entirety, considering the easy availability and accessibility of the most updated SPC/prescribing information through a clear and prominent direct single click link and a very clear sign posting which stated, 'Further information on interactions with other medicinal products is available in the Eliquis SPC'.

Although the Alliance submitted that it did not consider there was a breach of Clause 7.2 because of the prominent availability of prescribing information and sign posting to consult this information for all interactions, it had, nevertheless, decided to add this interaction to the webpage for additional clarity.

The Alliance submitted that the webpage in question met the requirements of Clause 3.2. The promotional content was in line with the marketing authorization and was not inconsistent with the particulars listed in the SPC/prescribing information. No promotional material suggested that Eliquis could be safely used in conjunction with SSRIs/SNRIs. There was a short summary of the haemorrhage risks, and a final paragraph, which stated 'Further information on interactions with other medicinal products is available in the Eliquis SPC'. In addition, on scrolling down to the bottom of the page a link to the Eliquis SPC and prescribing information was provided.

The Alliance submitted that it had followed the requirements of Clause 4.4 of the Code, which stated that in the case of digital material the prescribing information must be provided either: by inclusion in the digital materials itself, or by way of a clear and prominent direct single click link. Based upon the above information, the Alliance denied a breach of Clause 3.2 as all requirements of that clause had been met.

The Alliance stated that patient safety was at the core of its culture and it took it as its ethical responsibility to adhere to best practices when it came to patient safety. In this particular example it had met all the internal standard operating procedures (SOPs) and Code requirements with a sense of urgency and responsibility. The Alliance stated that it followed strict internal SOPs for promotional material reviews, and approvals. The Alliance further submitted that it ensured that all of its signatories were properly trained; skills and knowledge were maintained via internal training and refresher sessions. Since the SPC update, the promotional materials were reviewed and re-approved as per the SOP to contain the most updated SPC and prescribing information. During this process, the content of a number of promotional materials was also updated to include interactions with SSRIs/SNRIs as noted above.

The webpage at issue always contained the most up-to-date SPC/prescribing information with a simple 'one click' easy access and a clear direction to the readers to review the full information regarding any warnings and precautions of use related to Eliquis.

Following the regulatory additions of SSRI and SNRI in Sections 4.4 and 4.5 of the SPC, the Alliance immediately updated the link to all materials to include this new information.

The Alliance submitted that it had a strong process in place for the review and approval of materials and the update of promotional materials following the above update to the SPC followed the robust SOP. The Alliance thus considered that high standards at all times were met and that there was no breach of Clause 9.1.

The Alliance denied any breach of Clause 2. The companies had taken all the steps according to their SOPs and requirements of the Code to ensure that they did not reduce the confidence in the industry.

**PANEL RULING**

The Panel noted that the website in question was for health professionals and was headed 'Practical Information To assist your daily practice'. The section giving guidance on special warnings and precautions for use referred to a number of factors to consider; the second factor listed was 'interaction with other medicinal products affecting haemostasis'. The information in this part of the website included the need to take care if patients were treated concomitantly with NSAIDs including aspirin and concluded that 'Further information on interactions with other medicinal products is available in the Eliquis SmPC'. The template for the website included links to the prescribing information, the adverse event reporting information, the SPC and to the patient information leaflet. At the end of the list of factors to consider was a reference to 'see Eliquis

SmPC for full prescribing information'.
The Panel noted the Alliance's submission that the links provided were to the amended SPC and prescribing information which had the information that care was to be taken if patients were treated concomitantly with SSRIs or SNRIs or NSAIDs including acetylsalicylic acid (Section 4.4) and that Eliquis should be used with caution when coadministered with SSRIs, SNRIs or NSAIDs (including acetylsalicylic acid) because these products typically increased the bleeding risk (Section 4.5).

The Panel considered that only referring to the cautions for coadministering NSAIDs and not referring to similar cautions with SSRIs or SNRIs on a detailed page about special warnings and precautions for use was misleading. There was an implication that all relevant interactions with other medicinal products affecting haemostasis were included and this was not so. The section at issue mentioned that further information on interactions with other medicinal products was available in the Eliquis SPC but this did not specifically refer to medicines which affected haemostasis. The Panel ruled a breach of Clause 7.2 of the Code. The Panel considered that although misleading, the omission did not necessarily mean that the material was inconsistent with the SPC and therefore ruled no breach of Clause 3.2 of the Code.

The Panel considered that the companies had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted its comments above and that neither SSRIs nor SNRIs were contra indicated with Eliquis and health professionals would be cautious when initiating any therapy. The Panel considered that in the particular circumstances of this case the omission of information about the need for care if SSRIs or SNRIs were coadministered with Eliquis did not warrant a ruling of a breach of Clause 2 which was reserved as a sign of particular censure. The Panel therefore ruled no breach of Clause 2 of the Code.

**Complaint received** **5 February 2019**

**Case completed** **2 May 2019**

**CASE AUTH/3157/2/19**

# VOLUNTARY ADMISSION BY ASTRAZENECA

## Substantiation of a claim for Fluenz Tetra

**AstraZeneca voluntarily admitted that a claim on the Fluenz Tetra (live attenuated influenza vaccine (LAIV)) website (fluenztetra.co.uk) could not be substantiated by the reference cited.**

**As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint the matter was taken up with AstraZeneca.**

**The detailed response from AstraZeneca is given below.**

**The Panel noted the statement at issue, 'Approximately 125.6 million doses of nasal spray flu vaccine (trivalent and quadrivalent) have been distributed worldwide since the 2003/04 flu season until the end of the 2017/18 flu season [data on file], and there have been no laboratory-confirmed reports of LAIV virus transmission or illness associated with LAIV virus transmission [Izurieta *et al* 2005]', appeared on the Fluenz Tetra nasal spray website and in a Q&A booklet aimed at health professionals.**

**The statement was part of a response to the question 'What is the transmission risk?' on the website.**

**The Q&A document question 'Is there a risk of transmitting Fluenz Tetra viruses?' was followed by 'Vaccine recipients should be informed that Fluenz Tetra is a live attenuated influenza vaccine and has the potential for transmission to immunocompromised contacts'. This was followed by the statement at issue.**

**The Panel noted AstraZeneca's submission that the impression given by the statement at issue could not be supported by the references given and that, to date, there had been few published or documented cases of secondary transmission from vaccinated individuals to no-vaccinated individuals; whilst the numbers were very small, there had been cases.**

**The Panel considered that the claim was misleading and could not be substantiated and breaches of the Code were ruled including that AstraZeneca had failed to maintain high standards as acknowledged by AstraZeneca.**

AstraZeneca voluntarily admitted that a claim on the Fluenz Tetra (live attenuated influenza vaccine (LAIV)) website (fluenztetra.co.uk) could not be substantiated by the reference cited.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with AstraZeneca.

**VOLUNTARY ADMISSION**

AstraZeneca explained that it had potentially breached Clauses 7.2, 7.4 and 9.1 of the 2016 Code with regard to the health professional section of Fluenz Tetra nasal spray website and a questions and answers (Q&A) booklet, also aimed at health professionals.

AstraZeneca stated that it discovered the potential breaches on 6 December 2018, after a member of the public enquired about transmission data on the Fluenz Tetra website. This was a promotional website for health professionals only, which contained learning modules on Fluenz. To access the modules, visitors had to declare whether they were a health professional or member of public; no access was granted to members of the public.

The enquiry centred on why transmission information contained in the US prescribing information was not on the UK website. The particular information in question was not included in the EU approved Quality Review of Documents (QRD) and subsequently the UK summary of product characteristics (SPC) in line with the assessment by the European Medicines Agency (EMA).

During the investigation it was noticed that in the section on the website about the risk of transmission of the live attenuated virus from a recipient to an immunocompromised individual, there was a subsequent page that discussed transmission from vaccine recipients to healthy individuals. This statement also appeared in the Q&A booklet.

The statement read as follows:

> 'Approximately 125.6 million doses of nasal spray flu vaccine (trivalent and quadrivalent) have been distributed worldwide since the 2003/04 flu season until the end of the 2017/18 flu season [data on file], and there have been no laboratory-confirmed reports of LAIV virus transmission or illness associated with LAIV virus transmission [Izurieta *et al* 2005].'

AstraZeneca stated that the claim suggested that all reported cases of influenza were investigated to exclude transmission from other sources than the wild type form of the virus. This was not the case and could not be substantiated by the two references cited.

AstraZeneca stated that, to date, there had been few published or documented cases of secondary transmission from vaccinated individuals to no-vaccinated individuals but the fact remained whilst the numbers were very small there had been cases.

AstraZeneca stated that it was committed to ensuring it upheld the highest of standards and therefore it had: removed the statement in question and associated pages from the website on 12 December 2018; recalled the Q&A booklet on 13 December 2018; and retrained the individuals involved.

The material had been certified in line with standard operating procedures. AstraZeneca was disappointed that the company's normal attention to detail was not demonstrated when these items were reviewed.

AstraZeneca stated that the claim was in breach of Clauses 7.2 and 7.4 of the Code and that the company, in this instance, had not maintained high standards in line with its values and therefore had also breached Clause 9.1.

**RESPONSE**

AstraZeneca stated that the website and Q&A document were used as support material for health professionals for the 2018/19 flu season. The webpages at issue were part of an online training module. The Q&A booklet was for use by health professionals to support use of Fluenz, which was part of the childhood flu immunisation programme.

**PANEL RULING**

The Panel noted the statement at issue: 'Approximately 125.6 million doses of nasal spray flu vaccine (trivalent and quadrivalent) have been distributed worldwide since the 2003/04 flu season until the end of the 2017/18 flu season [data on file], and there have been no laboratory-confirmed reports of LAIV virus transmission or illness associated with LAIV virus transmission [Izurieta *et al* 2005]', which appeared on the Fluenz Tetra nasal spray website and in a Q&A booklet aimed at health professionals. The statement was part of a response to a question on the website 'What is the transmission risk?'. The Q&A document question 'Is there a risk of transmitting Fluenz Tetra viruses?' was followed by 'Vaccine recipients should be informed that Fluenz Tetra is a live attenuated influenza vaccine and has the potential for transmission to immunocompromised contacts'. This was followed by the statement at issue. The Panel noted AstraZeneca's submission that the impression given by the statement at issue could not be supported by the references given and that, to date, there had been few published or documented cases of secondary transmission from vaccinated individuals to no-vaccinated individuals; whilst the numbers were very small, there had been cases.

The Panel considered that the claim was misleading and could not be substantiated and ruled a breach of Clauses 7.2 and 7.4 as acknowledged by AstraZeneca.

The Panel considered that AstraZeneca had failed to maintain high standards and a breach of Clause 9.1 was ruled as acknowledged by AstraZeneca.

**Complaint received** **12 February 2019**

**Case completed** **8 May 2019**

# EMPLOYEE v SERVIER

## Arrangements for an advisory board

**A contactable complainant who described him/herself as a Servier employee complained about an advisory board on the management of metastatic colorectal cancer (mCRC) held on 23 June 2017. Servier marketed Lonsurf (trifluridine/tipiracil) which was used in certain patients with mCRC.**

**The complainant noted that advisory boards were meant to seek answers to unknown questions. The complainant alleged that from the beginning, two senior managers decided that the representatives should influence which health professionals should be invited to the advisory board. According to the complainant, one of the senior managers nominated health professionals who contributed heavily to sales and representatives suggested and got their favourite health professional to attend. The other senior manager then added a few health professionals that he/she knew well and who had attended a previous advisory board in 2016 on very similar topics. The complainant provided a copy of an email, between senior managers, sent after the advisory board, which he/she stated clearly acknowledged that attendees were selected by representatives and medical science liaison (MSL) staff. The complainant further alleged that a colleague in medical was put under extreme pressure from a more senior commercial manager to accept recommendations for health professional attendees.**

**With regard to content, the complainant explained that in 2017, some representatives pushed the idea that neutropenia, a common and at times serious side effect of Lonsurf, was a predictor of efficacy ie neutropenia meant that the medicine was working. This was challenged within the company and although some representatives were reprimanded by their local MSL for compromising patient safety, Servier continued to pursue the line that 'neutropenia was an indicator of efficacy'. At the advisory board in question, a number of case studies were discussed on this topic and clinicians shared examples of neutropenia and other adverse events; however, no effort was made to document these via pharmacovigilance or adverse event reporting. The complainant alleged that this clearly compromised patient safety.**

**The complainant stated that Servier put a positive spin on neutropenia because it had recently been reported that the incidence of neutropenia and febrile neutropenia was higher in clinical practice than previously documented. Rather than protecting patient safety and ensuring that representatives were adequately briefed on this finding, Servier promoted the idea that neutropenia was good and equalled efficacy. The complainant stated that evidence of this could be seen in the advisory board agenda and also in an email between senior managers in which it was stated that 'Neutropenia being a predictor (or not) of response' would be discussed. This showed the carefree attitude towards patient safety.**

**In summary, the complainant alleged that the advisory board was organised as a meeting for loyal users of Lonsurf and patient safety was compromised by not reporting adverse events. Representatives influenced attendee selection. The complainant further alleged that given the involvement of the commercial colleagues, the advisory board was a disguised promotional meeting; if this was not so then why did one senior manager in medical acknowledge the commercial functions in an email immediately after the advisory board, and not include a relevant medical colleague and team of MSLs?**

**The detailed response from Servier is given below.**

**The Panel noted that while it was acceptable for companies to pay health professionals and others for relevant advice, the arrangements for advisory boards had to comply with the Code. To be considered a legitimate advisory board the choice and number of participants should stand up to independent scrutiny; each should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the meeting.**

**The Panel noted the complainant's allegation that advisor selection was influenced by representatives and a senior manager who nominated health professionals who contributed heavily to sales. The Panel noted Servier's submission that one of the meeting objectives was to gain feedback on the practical use of Lonsurf and so advisors needed to have clinical experience with the medicine. In the Panel's view, it was not necessarily unacceptable for representatives to identify health professionals with relevant clinical experience to provide the clinical insights required. Regardless of the source of the recommendation, the criteria for selection must be directly related to the identified need and must not be, *inter alia,* an inducement to prescribe a medicine or a reward for previous prescriptions. The Panel noted Servier's submission that the final decision of who to invite lay with the medical department.**

**The Panel further noted the complainant's allegation that, to increase numbers, some health professionals were invited who had attended a very similar advisory board the previous year. The Panel noted Servier's submission that some of the attendees had indeed attended one or both of two previous Lonsurf advisory boards in January 2016 (before the product launch) and one of the two held in May 2016. The Panel noted the time-periods between the advisory boards, the different time-points in the product's lifecycle, and the largely different meeting objectives.**

**The Panel noted it comments above. A judgement had to be made on the available evidence. In the Panel's view, the complainant had not proved, on the balance of probabilities, that the selection of advisors was not directly related to the identified need or that the selection was an inducement to prescribe, supply, administer, recommend, buy or sell any medicine. No breach of the Code was ruled.**

**The Panel was concerned about the complainant's serious allegation that one manager was put under extreme pressure to accept recommendations for attendees from a more senior manager but noted that he/she had provided no evidence in this regard. The Panel considered that the complainant had not discharged the burden of proof and no breach of the Code was ruled.**

**The Panel noted the allegation that promoting neutropenia with Lonsurf as a predictor/indicator of response at the meeting demonstrated the company's carefree attitude towards patient safety. The complainant provided a copy of a presentation used at the meeting entitled 'Neutropenia – is it a predictor of response to trifluridine/tipiracil?'. The Panel noted that the objectives of the advisory board did not include obtaining feedback on neutropenia being a predictor of response. This topic was allocated 45 minutes on the agenda, including a 10-minute presentation. The Panel noted Servier's submission that the conclusion in the executive summary of the meeting minutes stated: 'Neutropenia is a manageable toxicity, but certainly not a predictor of response, but (it) is more of a reflection that an adequate dose has been given. Observations of improved overall survival (OS) and progression free survival (PFS) with the neutropenia cohort is more likely a testimony to them being a biologically different group, and not strong enough evidence to change clinical practice i.e. to induce neutropenia in patients who don't experience it'.**

**The Panel was concerned to note that the briefing documents to this session's speaker and to the meeting chair stated: 'To their knowledge does any company leverage this information in the promotion of their products?' and 'If a patient did not experience neutropenia what would this mean for the prescribing of trifluridine/tipiracil?'.**

**In the Panel's view, Servier intended to get feedback on neutropenia as a predictor of response with Lonsurf, including use of such a claim in the promotion of Lonsurf. Feedback from the advisors included 'A degree of caution should be exercised if using this argument commercially …' and 'These observations of improved [progression free survival] and [overall survival] do not suggest that clinicians should induce neutropenia in patients who don't present with it (i.e. by increasing the dose) for improved outcomes'.**

**Whilst the Panel had serious concerns about the acceptability of claiming that neutropenia was a predictor of response, it considered that it was not necessarily unacceptable to discuss the clinical data in an advisory board in order to gain advice. There was no evidence that the claim was used to promote Lonsurf. Noting its comments above, the Panel considered that the complainant had not discharged the burden of proof in this regard and ruled no breach of the Code.**

**The Panel then considered the allegation that Servier had not reported the adverse events from patient cases. The title page of the clinical case presentation slides used at the meeting included the statement 'Please note that all of the following case scenarios are hypothetical'. The speaker's briefing document stated that this section of the advisory board was not to prompt the discussion of adverse events ie events related to a specific patient. It also stated that if any events were discussed, Servier would have to follow them up. The chair's briefing had similar statements and that the speaker would make attendees aware of the pharmacovigilance statement. The Panel noted Servier's submission that, from the meeting minutes, there was no specific patient or group of patients discussed, and adverse events were discussed only in general terms prompted by the hypothetical cases presented.**

**The Panel noted the importance of reporting adverse events and that Servier had briefed the speaker and chairman. It appeared that if adverse events that required reporting had been raised, relevant personnel knew what to do. The Panel considered that the evidence supplied by the complainant did not show, on the balance of probabilities, that Servier had not met the requirements of the Code in relation to adverse event reporting and therefore ruled no breach of the Code.**

**The Panel noted the further allegation that some Servier representatives had promoted the concept of neutropenia with Lonsurf as an indicator of efficacy and that this compromised patient safety. The Panel noted that, *inter alia,* briefing material must not advocate, directly or indirectly, any course of action which would be likely to lead to a breach of the Code. The Panel noted Servier's submission that its sales materials and briefing documents did not mention, claim or compare any evidence that neutropenia was an indicator of efficacy and that it had no record of representatives being reprimanded for such activity as alleged. The Panel considered that as the complainant had provided no evidence to support this allegation, he/she had not discharged the burden of proof. The Panel therefore ruled no breach of the Code.**

**The Panel noted the complainant's general allegation that the advisory board in question was a disguised promotional meeting for loyal Lonsurf customers. The Panel noted that although a disputed email was not copied to the MSLs or a relevant member of the medical team and the medical team member was not acknowledged in the email, this did not in itself indicate that the advisory board was a disguised promotional meeting as alleged. Nor did the role of commercial colleagues necessarily indicate that the advisory board was a disguised promotional meeting as alleged.**

**The Panel noted that ten health professionals and three Servier employees attended the meeting in**

**question. The Panel noted the meeting objectives, the expected outputs in the certified rationale document and Servier's submission regarding the expertise and experience of the advisors selected in relation to the advice sought. Servier had retrospectively analysed sales data and found no evidence that any of the advisors were 'loyal users of Lonsurf' as alleged.**

**The Panel noted from the agenda that just over 80% of the meeting which was held from 10am-4pm was allocated to discussion. There was 40 minutes of presentation time. Feedback and advice obtained from the advisory board was documented in the meeting executive summary along with actions for Servier.**

**The Panel noted its comments above. A judgement had to be made on the evidence provided by the parties. Whilst there were some concerns, in the Panel's view, the complainant had not proved, on the balance of probabilities, that the advisory board meeting was disguised promotion and no breach of the Code was ruled.**

**The Panel noted that Clause 2 was used as a sign of particular censure and reserved for such use. The Panel noted its comments and rulings above and ruled no breach of Clause 2.**

A contactable complainant who described him/herself as a Servier employee complained about an advisory board on the management of metastatic colorectal cancer (mCRC) held by Servier on 23 June 2017. Servier marketed Lonsurf (trifluridine/tipiracil) which was used in certain patients with mCRC.

**COMPLAINT**

**A Selection of advisors**

The complainant noted that advisory boards were meant to have a very specific purpose of seeking answers to unknown questions. The complainant alleged that from the beginning, two senior managers decided that the representatives should take an active role in determining which health professionals should be invited to this advisory board. According to the complainant, one of the senior managers (commercial) decided to nominate a range of health professionals who contributed heavily to sales and each representative suggested and got their favourite health professional to attend and then, to increase numbers, the other senior manager (medical) added a few health professionals that he/she knew well and who had attended a previous advisory board in 2016 on very similar topics. The complainant stated that an email between senior managers immediately after the advisory board, showed clear acknowledgement that the attendees were selected by the representatives and medical science liaison (MSL) staff. The complainant stated that no member of medical affairs other than the sender was included in the email as only the commercial senior manager and the representatives had been consulted on advisor selection and not the MSLs. At the time the manager of the oncology MSLs was not included in the email and was put under extreme pressure from a more senior commercial manager to accept recommendations for health professional attendees. The complainant noted that the senior manager who sent the email acknowledged the role of the representatives in selecting advisors and copied in the commercial senior manager who had attended the advisory board in full; his/her attendance was challenged given that part of his/her role was to serve as a sales manager in a named disease area. The complainant stated that although the email implied that the commercial senior manager was just copied in for information purposes, he/she had, in fact, heavily influenced the selection of attendees and the content of the advisory board.

**B Discussion of neutropenia as an indicator of response**

The complainant further stated that the commercial senior manager, endorsed by the medical senior manager, attended the advisory board and discussed neutropenia as an indicator of response.

The complainant explained that in early 2017, some representatives promoted the idea that neutropenia, a common and at times serious side effect of Lonsurf, was a predictor of efficacy ie neutropenia meant that the medicine was working. This was challenged by the MSLs, and several representatives were reprimanded by their local MSL for compromising patient safety. The relevant manager within the company was informed about this reckless behaviour by some representatives, but Servier continued to pursue the line that 'neutropenia was an indicator of efficacy'.

At this advisory board, a number of case studies were discussed on this topic and clinicians openly shared their real-life patient examples of neutropenia and other adverse events; however, no effort was made to document or report these via pharmacovigilance or adverse event reporting. The complainant alleged that this clearly compromised patient safety.

The complainant stated that Servier put a positive spin on neutropenia because a recent clinical audit conducted by some UK sites on the Early Access Programme had found that the incidence of neutropenia and febrile neutropenia was higher in clinical practice than previously reported in the RECOURSE study. The complainant alleged that rather than protecting patient safety and ensuring that the representatives were given adequate briefing on this finding, Servier thought it would be a good idea to promote the idea that neutropenia was good and equalled efficacy.

The complainant stated that clear evidence of this could be seen in the advisory board agenda and in the email between senior managers referred to above which stated that one of three discussion topics would be the idea of 'Neutropenia being a predictor (or not) of response'. This again showed the carefree attitude towards patient safety ie trying to portray drug toxicity as an indicator of response and making no effort to report adverse events from health professional

cases. References and data promoting this idea were presented at the advisory board.

**C General allegations**

In summary, the complainant alleged that the advisory board was organised under the disguise of a meeting meant for loyal users of Lonsurf and patient safety was compromised by not reporting adverse events in the neutropenia session and discussion. Representatives influenced attendee selection and were thanked by the senior manager (medical) which clearly showed that this was a disguised promotional meeting heavily influenced and organised by the commercial senior manager and the representatives. The complainant queried that if this was not the case then why did the senior manager (medical) acknowledge the commercial senior manager and representatives in the email immediately after the advisory board, and not include a relevant medical colleague and team of MSLs.

When writing to Servier, the Authority asked it to consider the requirements of Clauses 2, 7.2, 7.4, 7.9, 9.1, 12.1, 15.9, 23.1 and 25.1 of the 2016 Code.

**RESPONSE**

Servier submitted that the advisory board in question was held to answer specific questions about the treatment of metastatic colorectal cancer (mCRC) and use of Lonsurf which received its marketing authorization from the European Medicines Agency (EMA) in April 2016 for heavily pre-treated patients with mCRC.

Servier recognised the importance of maintaining high standards and upholding regulatory values when conducting an advisory board, particularly given the compliance difficulties that companies could experience with these meetings and the high profile given to them in the UK recently. As such, Servier stated that it had taken the complaint very seriously and had thoroughly investigated it despite the difficulties of doing so given that the company was not told about any concerns regarding the advisory board until more than 18 months after it had taken place. Two key people had since left the company and so it was not feasible to interview them. Having conducted its investigation, however, Servier stated it was satisfied that the advisory board in question was a legitimate and compliant meeting.

**Legitimate business need for advisory board**

Servier refuted the complainant's allegation that the selection of participants was heavily influenced by commercial (sales) considerations and submitted that the advisors were chosen on the basis of their ability to help the company meet the objectives of the meeting by answering specific questions which related to the following four topics:

**1 Develop a better understanding of re-challenge.**

Servier explained that the European Society of Medical Oncology (ESMO) guidelines recommended a continuum of care approach. Patients would be given a successive sequence of active agents (eg chemotherapy alone or in combination with biological agents) until they progressed or could not continue due to toxicity. Therefore, as treatment improved there was an increasing proportion of heavily pre-treated patients with advanced disease who became eligible to receive third- and fourth-line care. Re-challenge was the strategy of re-introducing, after an intervening treatment, a previous therapy to which the tumour had been resistant. Despite recommendations for agents such as Lonsurf or regorafenib to be introduced as a third-line option prior to re-challenge, re-challenge remained a prevalent treatment choice in the UK; market research from 2017 reported that clinicians treated 28% of patients with re-challenge. It was therefore imperative that Servier understood why clinicians chose treatment options other than those recommended in the guidelines.

**2 Practical issues with Lonsurf in clinical practice; dose delays and reductions, and adverse event management**

Servier explained that Lonsurf was dosed according to body surface area and, based on the toxicity experienced by the patient, might be delayed, reduced or stopped. Its dosing schedule was different from other oral chemotherapies (eg capecitabine) which caused some initial confusion about administration. Ensuring that administration was consistent with the recommendations in the summary of product characteristics (SPC) was key to ensure patients received appropriate care. Many of the Lonsurf sales materials (copies provided) related to appropriate dosing eg when to stop, delay or reduce dose. Therefore, at just one year after launch of the product, another key objective of this advisory board was to ensure there was no unmet need for further guidance from the company to clinicians on this topic.

**3 Should Servier conduct a Phase IV observational study?**

Servier submitted that it had asked this question because the global team had proposed a Phase IV observational study in patients with mCRC to include collecting quality of life data. To help ensure that the study would generate information that would be useful to UK clinicians when managing their patients, Servier UK wanted to gain feedback regarding this proposed study and whether there were any potential amendments that should be made or gain insight on whether Servier should support alternative studies.

**4 Was neutropenia an indicator of efficacy?**

This question was asked because the patient population who required treatment with Lonsurf had a very poor prognosis and although a significant proportion of them would receive clinical benefit from Lonsurf, some would not. Thus, clinicians were often keen for any data on prognostic factors that would help them to pre-select those more likely to benefit from Lonsurf treatment. There had been several publications (Kasi *et al* 2016 and Ohtsu *et al* 2016) which had associated a survival benefit for

patients who experienced neutropenia while treated with Lonsurf. This was an exploratory question on whether neutropenia was a predictor of efficacy. Servier submitted that these questions were a legitimate reason to hold an advisory board meeting and that an advisory board would be the most appropriate method to help answer them as they required a range of extensive qualitative opinions from experts within the field. The meeting was structured in order to ensure that the advisors had ample time to discuss the questions and provide meaningful advice to the company, as demonstrated by the meeting materials and outputs (copies provided). A meeting report was generated which included various outputs. This report which included feedback on a Global Phase IV study and other study suggestions, was circulated within the UK team and to Servier's global colleagues.

**A Selection of advisors**

Servier refuted the allegation that health professionals were selected based on any promotional intent. The nature of the questions that the advisory board sought to answer required the advisors to have specific knowledge and experience and selection was made on this basis.

The invited clinicians were all experienced with a wide range of clinical and trial experience that allowed them to contribute meaningfully to the advisory board discussions. The advisory board rationale document noted that advisors selected would be: oncologists experienced in re-challenge as a treatment strategy; those who had used Lonsurf clinically and in the third-line mCRC setting; experienced researchers or investigators in mCRC or, as a minimum, considered suitable to be investigators and researchers.

There were 10 attendees who were paid in line with Servier's standard operating procedures (SOPs) (copies provided). Servier considered that the payments represented fair market value for the advisors' level of experience and time given to the advisory board (honoraria and travel expenses for each advisor was provided).

The selection of the attendees was based on the above criteria and was the responsibility of medical and not the responsibility of a commercial manager. Servier stated that it had no evidence to support the allegation that a medical colleague was put under extreme pressure from the more senior commercial manager to accept recommendations for attendees; nothing was reported to its HR department that would corroborate it.

Servier submitted that none of the representatives interviewed could recall recommending any advisors for the advisory board although the company acknowledged that they might have either forgotten (given the timeframe) or felt uncomfortable divulging this information (despite reassurance). It would not necessarily be unreasonable for field staff to give recommendations to ensure that advisors with the relevant experience (including prescribing experience) were identified. However, the final decision on who to invite was medical's responsibility. Servier's standard for selection would be based solely on the attendees' scientific and medical expertise and the anticipated value of their contributions to the advisory board, in line with the rationale document. The invitation was prepared and sent out by medical (copy provided).

Servier stated that it could not confirm the authenticity of the email referred to by the complainant and allegedly sent by medical 18 months ago as it was not recoverable from the accounts of any of the three staff who were included in the message; two of the staff had subsequently left the company. The email stated that both the representatives and the MSLs 'suggested [the attendees] would give us useful insights'. Servier submitted that contrary to the complainant's allegation that the advisory board was a disguised promotional meeting, the wording supported its contention that advisory board members were chosen for their medical and scientific insights, irrespective of the alleged source of the recommendations.

Servier submitted that it had retrospectively analysed which sales territories the attendees came from (copy of analysis provided) and had not been able to discern any evidence that advisors were selected due to any commercial reason or that they were 'loyal users of Lonsurf' as alleged. One advisor had extensive clinical trial experience but his/her hospital had bought no Lonsurf in the 6 months before the advisory board.

With regard to attendees' attendance at previous Lonsurf advisory boards, Servier noted that it had held four such meetings (copies of agendas and details of the meeting objectives were provided) two in January 2016 (before the product was licensed) and two in May 2016 (after the product was licensed), ie more than a year before the meeting in question. Servier submitted that each of the previous advisory boards explored different business needs from the one in question, at a different stage of the company's knowledge and understanding of the environment. Servier noted that some of the attendees of the meeting in question had already provided advice at Servier advisory boards in 2016, most notably an advisory board held in January 2016, 18 months before the one in question, and prior to launch of the product; six clinicians had attended that meeting and the one now in question (two of the clinicians had also attended the other meeting in January 2016). At that time Servier would have had limited relationships with any clinicians. Those who attended were prominent and highly specialised in the field and thus able to effectively contribute to the discussion at an advisory board. Given their expertise and their proven ability to contribute meaningfully to an advisory board, Servier stated that it was not surprising to see that they were invited to attend a different advisory board asking different questions 18 months later. Servier submitted that one attendee at one of the May 2016 advisory boards had attended the meeting now at issue. None of the attendees at the second meeting in May 2016 attended the meeting now at issue.

Servier submitted that along with the ten invited clinicians, three Servier staff attended the advisory board in question – two from medical and one commercial employee - all of whom had since left Servier (copies of job descriptions provided).

Servier stated that the complainant had questioned the legitimacy of the commercial senior manager's attendance at the advisory board as he/she had a role in management of the sales team. No-one had questioned his/her presence or conduct at the meeting at the time. The manager's role included oversight of the sales team but also, more notably, marketing strategy. As the questions the advisory board sought to answer directly impacted on marketing strategy, the senior manager was present to help ensure that the company obtained a clear understanding of the environment and challenges and that any advice that would help inform strategy was appropriately implemented. Thus, his/her attendance at the advisory board was to facilitate Servier's understanding of the answers to the questions.

Servier stated that in summary in relation to the selection of advisors:

- A clear agreement and rationale for the services rendered were put in place in advance of the commencement of the clinicians' services at the advisory board. Servier denied breaches of Clause 23.1.
- Servier had demonstrated a clear rationale for the selection of advisors to the advisory board meeting, who were then selected based on this criteria by medical. Servier denied breaches of Clause 23.1.
- This advisory board was not a 'token consultancy arrangement' but a legitimate and compliant meeting, for which the advisors were paid commensurate with their experience and time given. Servier denied breaches of Clause 23.1.
- Servier had maintained high standards throughout this process; it had adhered to Code requirements and company SOPs. Servier denied breaching Clause 9.1.

**B Discussion of neutropenia as an indicator of response**

Servier explained that the Early Access Program the complainant referred to was actually the named patient programme (NPP), where under guidance from the Medicines and Healthcare products Regulatory Agency (MHRA) for supply of unlicensed medicines, Lonsurf was available to UK patients for 8 months from November 2015. A retrospective audit of 78 patients from the NPP from 3 UK sites showed a similar overall survival benefit to that seen in the RECOURSE study (6.6 months vs 7.1 months in the RECOURSE study) but 40% of patients experienced neutropenia and 13% experienced febrile neutropenia vs 38% and 4% respectively in the RECOURSE study.

Servier submitted that it would not make any unsubstantiated claims and patient safety was a key priority at all times. Neutropenia was discussed at the advisory board because various published studies associated neutropenia as an indicator of efficacy for Lonsurf treatment. Servier submitted that this was a legitimate exploratory question to ask at an advisory board and so there was a 10-minute presentation asking 'Neutropenia: Is it a predictor of response with trifluridine/tipiracil?' using 8 slides, including the title slide, disclosures and summary slides. A further three slides discussed evidence of chemotherapy-induced neutropenia in general, not specifically related to Lonsurf, and two slides examined 2 different data sources that associated neutropenia with a survival benefit in patients treated with Lonsurf. There was 35 minutes allowed for discussion.

From the meeting minutes the conclusion in the executive summary was that:

> 'Neutropenia is a manageable toxicity, but certainly not a predictor of response, but (it) is more of a reflection that an adequate dose has been given. Observations of improved overall survival (OS) and progression free survival (PFS) with the neutropenia cohort is more likely a testimony to them being a biologically different group, and not strong enough evidence to change clinical practice i.e. to induce neutropenia in patients who don't experience it.'

Servier stated that in summary in relation to the content of the advisory board:

- The content of this presentation (and following discussion) was given in a clear objective and balanced manner and was not misleading. Servier denied a breach of Clause 7.2.
- All the information given to advisors could be substantiated. Servier denied a breach of Clause 7.4.
- The data presented reflected available evidence, and Servier did not try to mislead the advisors as to the toxicity profile of Lonsurf. Servier denied a breach of Clause 7.9.
- Servier had maintained high standards throughout this process by adhering to the Code and company processes. Servier denied a breach of Clause 9.1.

Servier stated that there was no evidence to support the allegation that representatives promoted neutropenia as an indicator of efficacy or that sales or briefing materials (copies provided) referred to neutropenia as such. There was no record of any representative being reprimanded by an MSL and none of the MSLs (including the MSL that had since left Servier) or the representatives consulted, nor a relevant manager, had any memory of this occurring.

Servier stated that in summary:

- Sales materials and briefing documents did not mention, claim or compare any evidence of neutropenia being an indicator of efficacy. Servier denied any breach of Clauses 7.2 and 7.4.
- Servier had maintained high standards throughout this process. Servier denied any breaches of Clause 9.1.

- No formal report of any kind of reprimand for any of the representatives compromising patient safety appeared to have been made, and none of the staff consulted were able to verify the veracity of this claim. Servier denied breaches of Clause 15.1.

**C General allegations**

Servier denied that the advisory board in question was held for any promotional intent, disguised or otherwise. Servier stated that it could be clearly demonstrated that:

- The meeting was organised and led by the medical affairs team, not the commercial;
- The advisory board was held to answer legitimate business questions as set out in the meeting rationale document and agenda;
- Attendees were selected based on their scientific and medical experience to be able to discuss and advise Servier on its business questions;
- The overall balance of the agenda between presentation and discussion time (excluding break and opening and closing times) was over 80% discussion time;
- Three presentations (copies provided) were given over the course of the day:

  **Presentation 1:** Rechallenge vs re-introduction – what does this mean in the third line mCRC setting? The 33-slide presentation was prepared by the presenting clinician (as part of the requirement for attendees to advise the company at this advisory board) and given over 20 minutes. It ran through guidelines and data on re-challenge. Within this, Lonsurf along with other therapeutic options was first mentioned on slide 13. Lonsurf was mentioned on 4 slides, and only factual information was presented; no claims were made.

  **Presentation 2:** Neutropenia: Is it a predictor of response with Lonsurf? This 8-slide presentation, also prepared by the presenting clinician was given over 10 minutes. It outlined evidence for neutropenia as a marker of efficacy in general chemotherapy and in 2 slides objectively outlined data which associated neutropenia with improved survival in patients treated with Lonsurf.

  **Presentation 3:** Potential future R&D options for Servier products. This 25-slide presentation was given over 10 minutes. It gave a run through of Lonsurf's current development program, without making any claims and solicited feedback on an observational study.

- The meeting minutes clearly recorded that Servier asked for advice and feedback and did not promote Lonsurf.

In relation to the allegations about patient safety, Servier categorically denied any wrong doing and had a firm commitment to patient safety. This included both adverse event reporting and ensuring that clinicians fully understood the toxicity profiles of Servier products and how to manage them appropriately.

Servier submitted that its pharmacovigilance department had robust systems in place to ensure all adverse events were reported and processed appropriately. This included annual training for all staff, including those who had attended the advisory board meeting in question (copy of training records provided). The company was confident that the highly experienced and trained staff who organized and attended the meeting would have reported any adverse event mentioned, in line with its pharmacovigilance SOP.

Servier submitted that as the advisory board included discussion on adverse event management and dosing guidelines, it was to be expected that this might elicit adverse event reports and the matter was discussed with Servier's pharmacovigilance department beforehand to ensure all appropriate action was taken. Following an email discussion with the pharmacovigilance department a briefing document was prepared for the relevant discussion that stated:

> 'Please make all attendees aware of the following important pharmacovigilance information:
>
> This section of the advisory board is not to prompt the discussion of adverse events, i.e. events related to a specific patient. If any events are discussed (or situations of special interest) that may be considered to fall into this category, Servier will have a requirement to follow these events up according to usual procedures (even if they have been reported by the Yellow Card Scheme).'

Servier stated that this showed that it was fully aware of the potential that adverse events might be discussed and was prepared to handle this appropriately. However, no adverse events were reported based on the discussions from this advisory board. There was no transcript of the meeting, but from the meeting minutes, although adverse events were discussed in general terms (prompted from the hypothetical case studies presented), no specific patient or group of patients were discussed. Servier noted that prior to the advisory board there were 17 reported adverse events from 7 of the attendees, including 13 neutropenia cases.

Servier stated that in summary it had:

- Demonstrated that the advisory board was clearly not held with any promotional intent, disguised or otherwise. Servier denied any breach of Clause 12.1.
- Shown that it had robust systems and training in place to capture all adverse events reported; that it made clear preparation prior to the advisory board to account for any adverse events reported; and that the advisory board was a legitimate and compliant non-promotional meeting. Servier denied breaching Clause 2.
- Maintained high standards throughout this process. Servier denied breaching Clause 9.1.
- Shown that it had robust systems and training in place to capture all adverse events reported; and that it made clear preparation prior to the advisory board to account for any adverse

events reported. Servier denied breaching Clause 25.1.

Servier submitted that the complainant had not given any evidence that would support his/her allegations that the advisory board was held with promotional intent or that patient safety was not prioritised. Servier submitted that it had provided detailed and robust evidence that demonstrated that the advisory board was an appropriate means of gaining information from advisors, and that patient safety was maintained throughout. Servier categorically denied all allegations in this complaint including a Clause 2.

In conclusion, Servier submitted that it had presented comprehensive arguments supported by evidence which demonstrated that it had complied with the Code in relation to the advisory board. Servier noted that the complainant's language was highly inflammatory and personal.

Following the Authority's receipt of Servier's response, the complainant provided annotated copies of the advisory board agenda, meeting rational document and slides from two sessions titled, 'Neutropenia - Is it a predictor of response to trifluridine/tipiracil?' and 'Lonsurf - clinical cases: What is your current approach to these scenarios?'. The case preparation manager provided this additional information to Servier for comment.

Servier stated that the complainant had provided an old and incomplete version of the advisory board rationale document. It had an old job reference number (used in a previous advisory board rationale document) and was clearly used as a template for the final approved version. The final approved version had been supplied by Servier in its initial response. Servier stated that the agenda and the PowerPoint presentation 'Is neutropenia an indicator of efficacy?' provided by the complainant were the final approved versions which were also supplied by Servier in its initial response.

Regarding the PowerPoint presentation 'Clinical cases: What is your current approach to these scenarios?', Servier submitted that due to an oversight this was mistakenly not previously supplied by Servier. This presentation was intended as a prompt to facilitate the discussion. It included three hypothetical case scenarios and posed questions such as: 'In your practice, what is your approach to the management of Grade 3-4 non-haematological toxicities e.g. fatigue?'. The presentation provided by the complainant was the final approved version but not in the correct order. Servier provided a copy of the final approved version of this presentation and stated that it had re-reviewed the materials previously sent and this was now the complete material list.

**PANEL RULING**

**A Selection of advisors**

The Panel noted that it was acceptable for companies to pay health professionals and others for relevant advice. Nonetheless, the arrangements for advisory board meetings had to comply with the Code, particularly Clause 23. To be considered a legitimate advisory board the choice and number of participants should stand up to independent scrutiny; each should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the meeting.

The Panel noted the complainant's allegation that advisor selection was influenced by representatives and a senior commercial manager who nominated health professionals who contributed heavily to sales. The Panel noted Servier's submission that one of the meeting objectives was to gain feedback on the practical issues with the use of Lonsurf, including dosing, stop and delay criterion, and therefore advisors needed to have clinical experience with Lonsurf in the third-line mCRC setting. The Panel noted that this was stated in the advisory board rationale document which was certified on 26 April 2017. The Panel further noted the email provided by the complainant which was allegedly sent by the medical senior manager after the meeting and stated that the advisors were '…a testament to the [representative] and MSLs who suggested they would give…[Servier] useful insights'.

In the Panel's view, it was not necessarily unacceptable for a company to ask its representatives for names of health professionals with relevant clinical experience, including with its medicine, who could therefore provide the clinical insights that the company needed. Regardless of the source of the recommendation, the criteria for selection must be directly related to the identified need and must not be, *inter alia*, an inducement to prescribe a medicine or a reward for previous prescriptions. The Panel noted Servier's submission that the final decision of who to invite was the responsibility of medical.

The Panel further noted the complainant's allegation that, to increase numbers, the senior medical manager invited health professionals who had attended a very similar advisory board the previous year. The Panel noted Servier's submission that it had held an advisory board in January 2016, prior to the launch of Lonsurf, which was attended by six of the ten clinicians who attended the advisory board in question. Servier had also held another advisory board in January 2016, which was attended by two of the clinicians who attended the advisory board in question, and had held a further two advisory boards in May 2016: one was attended by one clinician who attended the advisory board in question and the other was not attended by any clinicians from the advisory board in question. The Panel noted the time-periods between the advisory boards, the different time-points in the product's lifecycle, and the largely different meeting objectives.

The Panel noted it comments above. A judgement had to be made on the available evidence. In the Panel's view, the complainant had not proved, on the balance of probabilities, that the selection of advisors was not directly related to the identified need or that the selection was an inducement to

prescribe, supply, administer, recommend, buy or sell any medicine. The Panel therefore ruled no breach of Clause 23.1.

The Panel was concerned about the complainant's serious allegation that a medical colleague was put under extreme pressure to accept recommendations for attendees from the senior commercial manager but it noted that he/she had provided no evidence in this regard. The Panel considered that the complainant had not discharged the burden of proof and no breach of Clause 9.1 was ruled in this regard.

**B Discussion of neutropenia as an indicator of response**

The Panel noted the allegation that neutropenia with Lonsurf as a predictor/indicator of response was promoted at the advisory board and this demonstrated the company's carefree attitude towards patient safety. The complainant provided a copy of a PowerPoint presentation, which Servier acknowledged was the final approved version presented at the meeting and titled 'Neutropenia – is it a predictor of response to trifluridine/tipiracil?'. The Panel noted that the complainant had referred to a slide which stated that neutropenia after starting Lonsurf was associated with better prognosis in patients with refractory mCRC and alleged that this was a clear attempt to link an adverse event of Lonsurf to overall survival and progression free survival. The Panel noted the questions on the following slide: 'Are these findings clinically relevant?' and 'Is there a potential for utility of [chemotherapy induced neutropenia at 1 month] as a prognostic and/or predictive biomarker of Lonsurf for patients with refractory metastatic CRC?'.

The Panel noted that the objectives of the advisory board in the rationale document did not include obtaining feedback on the topic of neutropenia being a predictor of response. This topic was allocated 45 minutes on the agenda, including a 10-minute presentation. The Panel noted Servier's submission that the conclusion in the executive summary of the meeting minutes stated:

> 'Neutropenia is a manageable toxicity, but certainly not a predictor of response, but (it) is more of a reflection that an adequate dose has been given. Observations of improved overall survival (OS) and progression free survival (PFS) with the neutropenia cohort is more likely a testimony to them being a biologically different group, and not strong enough evidence to change clinical practice i.e. to induce neutropenia in patients who don't experience it.'

The Panel was concerned to note that the briefing documents to this session's speaker and to the meeting chair stated: 'To their knowledge does any company leverage this information in the promotion of their products?' and 'If a patient did not experience neutropenia what would this mean for the prescribing of trifluridine/tipiracil?'.

In the Panel's view, Servier intended to get feedback on neutropenia as a predictor of response with Lonsurf, including use of such a claim in the promotion of Lonsurf. The Panel noted the documented feedback from the advisors which stated: 'A degree of caution should be exercised if using this argument commercially…' and 'These observations of improved PFS [progression free survival] and OS [overall survival] do not suggest that clinicians should induce neutropenia in patients who don't present with it (i.e. by increasing the dose) for improved outcomes'.

Whilst the Panel had serious concerns about the acceptability of using a claim about neutropenia being a predictor of response, it considered that it was not necessarily unacceptable for a company to discuss the clinical data in an advisory board in order to gain advice from attendees. There was no evidence that the claim was used to promote Lonsurf. Noting its comments above, the Panel considered that the complainant had not discharged the burden of proof in this regard and ruled no breach of Clauses 7.2, 7.4, 7.9 and 9.1.

The Panel then considered the allegation that Servier made no attempt to report the adverse events from patient cases in the advisory board. The Panel noted with concern that the clinical case presentation slides were only provided by the complainant and had not been provided by Servier in its initial response. The slides included the following statement on the title page: 'Please note that all of the following case scenarios are hypothetical'. The complainant had annotated the document to state that during the presentation the health professionals were asked to share examples of cases with neutropenia and no attempt was made to report adverse events. The Panel noted Servier's submission that prior to the advisory board there were 17 reported adverse events from 7 of the attendees, including 13 neutropenia cases, and the fact that the advisory board might elicit adverse event reports was discussed with the company's pharmacovigilance department prior to the meeting and a statement was added to the briefing documents. The speaker's briefing document stated that this section of the advisory board was not to prompt the discussion of adverse events ie events related to a specific patient. It also stated that if any events were discussed, Servier would have to follow these up. The chair's briefing had similar statements and that the speaker would make attendees aware of the pharmacovigilance statement. The Panel noted Servier's submission that, from the meeting minutes, there was no specific patient or group of patients discussed, and adverse events were discussed only in general terms prompted by the hypothetical cases presented.

The Panel noted the importance of reporting adverse events and that Servier had briefed the speaker and chairman. It appeared that if adverse events that required reporting had been raised at the advisory board, Servier and the meeting chair and speaker knew what action to take. The Panel considered that the evidence supplied by the complainant did not show, on the balance of probabilities, that Servier had not met the requirements of the Code in relation to adverse event reporting and therefore ruled no breach of Clauses 9.1 and 25.1.

The Panel noted the further allegation that some Servier representatives had promoted the concept of neutropenia with Lonsurf as an indicator of efficacy and that this compromised patient safety. The Panel noted that briefing material must comply with the relevant requirements of the Code and must not advocate, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code. The Panel noted Servier's submission that its sales materials and briefing documents did not mention, claim or compare any evidence that neutropenia was an indicator of efficacy. Further Servier stated it had no record of representatives being reprimanded for such activity as alleged by the complainant. The Panel considered that as the complainant had provided no evidence to support this allegation, he/she had not discharged the burden of proof. The Panel therefore ruled no breach of Clauses 7.2, 7.4, 7.9, 9.1 and 15.9 in this regard.

**C General allegations**

The Panel noted the complainant's general allegation that the advisory board in question was a disguised promotional meeting for loyal Lonsurf customers. The complainant queried that if the advisory board was not a disguised promotional meeting then why did the senior medical manager acknowledge the senior commercial manager and representatives in an email immediately after the advisory board, and not include a medical colleague and the team of MSLs.

The Panel noted that the disputed email was not copied to the MSLs or the medical colleague, however, the MSLs were mentioned in this email. The Panel considered that although the medical colleague was not acknowledged by the senior medical manager in the disputed email, this did not in itself indicate that the advisory board was a disguised promotional meeting as alleged. Nor did the role of the senior commercial manager and the representatives necessarily indicate that the advisory board was a disguised promotional meeting as alleged.

The Panel noted that there were ten health professionals and three Servier employees at the meeting in question. The Panel noted the meeting objectives and expected outputs in the certified rationale document. The Panel further noted Servier's submission regarding the expertise and experience of the advisors selected in relation to the advice sought. Servier had retrospectively analysed relevant sales data and submitted that it found no evidence that the advisors were 'loyal users of Lonsurf'; one advisor had extensive clinical trial experience but his/her hospital had not bought Lonsurf in the 6 months before the advisory board.

The Panel noted from the agenda that the advisory board started at 10am and finished at 4pm. Excluding introductions, lunch and meeting close, just over 80% of the time on the agenda was allocated to discussion. It appeared to the Panel that there were four presentations consisting of a total of 87 slides. The Panel queried whether so many slides were needed given that only 40 minutes of presentation time was on the agenda. The Panel noted Servier's submission that many of these slides built on each other, were one sentence asking a question or were title slides.

Feedback and advice obtained from the advisory board was documented in the meeting executive summary along with actions for Servier.

The Panel noted its comments above. A judgement had to be made on the evidence provided by the parties. Whilst the Panel had some concerns, in its view the complainant had not proved, on the balance of probabilities, that the advisory board meeting was disguised promotion and no breach of Clause 12.1 was ruled.

The Panel noted that Clause 2 was used as a sign of particular censure and reserved for such use. The Panel noted its comments and rulings above and ruled no breach of Clause 2.

**Complaint received** **5 February 2019**

**Case completed** **30 May 2019**

CASE AUTH/3161/2/19

# EMPLOYEE v LEO PHARMA

## Alleged promotional practices

**A named, non-contactable, current employee of Leo Pharma complained about some of the company's promotional practices.**

**The complainant was concerned that the company was breaching the Code because it:**

- **encouraged representatives to visit doctors five times a year ie more often than the allowed 3 unsolicited visits;**
- **did audits only for customers that used the company's products;**
- **did not put speaker slides through the medial legal approval process;**
- **encouraged representatives not to report adverse reactions for the company's medicines;**
- **encouraged representatives to email customers without their permission.**

**The detailed response from Leo is given below.**

**The Panel noted that the complainant only provided brief details about his/her complaint. There were no attachments provided to support the allegations. A complainant had the burden of proving their complaint on the balance of probabilities. It considered each allegation as follows:**

**1 Visits to doctors**

**The Panel considered that there was no evidence before it that the actual number of calls made on a doctor or other prescriber by a representative had breached the requirements of the Code. However, the Panel was concerned about the representative briefing material.**

**The Panel noted that the topical dermatology customer segmentation plan slides which referred to call frequency did not differentiate between an unsolicited call and a 'contact' as defined by Leo and made no reference to the Code requirements. The Panel considered that the slides should have clearly set out the position. Although it was helpful to remind representatives of the Code requirements verbally, in a follow-up email and in the SOP, in the Panel's view, each representative briefing that related to call frequency needed to stand alone and should have reiterated the Code requirements and definitions of a call versus a 'contact' as defined by Leo.**

**The Panel considered that the reference to call frequencies of 4 and 5 for health professionals in the topical dermatology customer segmentation slides, without any definition of a call or reiteration of the Code requirements, meant that, on the balance of probabilities, the briefing material advocated a course of action likely to lead to a breach of the Code and the Panel ruled a breach of the Code.**

**On balance, the Panel did not consider that Leo had failed to maintain high standards and ruled no breach.**

**2 Audits**

**The Panel considered that the allegation was unclear. It was not for the Panel to infer detailed reasons to support allegations. Complainants needed to provide sufficient detail so that the respondent company and the Panel could clearly understand the concerns. Further it was for the complainant to establish his/her case on the balance of probabilities. It was not necessarily a breach of the Code for audits to be linked to the use of a medicine; all the relevant circumstances would need to be considered. The Panel considered that the very general nature of the allegation and the lack of evidence was such that the complainant had not discharged his/her burden of proof. The Panel therefore ruled no breach of the Code including Clause 2 in this regard.**

**3 Speaker slides**

**The Panel noted that the complainant had not referred to any specific speaker slides. The Panel noted Leo's submission that its processes require promotional speaker slides to be certified. The Panel noted relevant details from Leo's standard operating procedure (SOP). The Panel considered that, based on the evidence before it, the complainant had not proved, on the balance of probabilities, that speaker slides had not been appropriately approved as required by the Code. The Panel thus ruled no breach in this regard.**

**4 Adverse event reporting**

**The Panel noted Leo's submission that all field force staff undertook pharmacovigilance training prior to commencing promotional activities and annual pharmacovigilance training was conducted for all staff including the field force. The Panel further noted Leo's submission that the training clearly laid out the expectation to report all adverse events, other experiences and product complaints for all Leo medicines, even if it was an expected event documented in the summary of product characteristics (SPC).**

**The Panel noted that the complainant had provided no evidence in support of his/her allegation that the field force was encouraged not to report adverse reactions. The Panel considered that, based on the evidence before it, the complainant had not proved, on the balance of probabilities, that there had been a breach of the Code in this regard and therefore ruled no breach.**

**5 Emails to customers**

**The Panel noted that the complainant had not referred to any specific instances or provided any evidence in support of his/her allegation that representatives were encouraged to email customers without their permission. The Panel noted relevant details in Leo's SOP. Further that it was not possible for a representative to send a Leo approved promotional email outside of the customer relationship management system and that the system itself would not issue an email without documented prior consent for the receipt of promotional information. The Panel considered that, based on the evidence before it, the complainant had not proved, on the balance of probabilities, that representatives were encouraged to email customers without their permission and therefore ruled no breach in this regard.**

A named, non-contactable, current employee of Leo Pharma complained about some of the company's promotional practices.

**COMPLAINT**

The complainant was concerned that the company was breaching the Code because it:

- encouraged representatives to visit doctors five times a year ie more often than the allowed 3 unsolicited visits;
- did audits only for customers that used the company's products;
- did not put speaker slides through the medial legal approval process;
- encouraged representatives not to report adverse reactions for the company's medicines;
- encouraged representatives to email customers without their permission.

When writing to Leo, the Authority asked it to bear in mind the requirements of Clauses 2, 9.1, 9.9, 14.1, 15.6, 15.9, 19.1 and 19.2 of the 2016 Code.

**RESPONSE**

Leo Pharma submitted that it took the Code extremely seriously and had a range of detailed procedures and training in place to ensure compliance with it, including for activities undertaken by representatives.

The company noted that the complainant had the burden of proving his/her complaint and that he/she had raised general points about procedures without referring to any one particular or specific instance/activity/material of concern, nor to any brand or therapy area and had not provided any evidence in support of the allegations.

Leo Pharma stated it had considered all therapy area business units in the UK and its investigations had covered all field force activities within those business units ie bio-dermatology, topical dermatology, thrombosis and market access. The investigations into each area included, but were not limited to; interviews with individuals (eg business unit head, head of sales etc), current standard operating procedures (SOPs) and work instructions (WIs), internal systems (eg PromoMats) and internal governance.

**1 Visits by representatives**

Leo stated that it had three therapy area teams in the UK; topical dermatology, bio-dermatology and thrombosis. The company had reviewed relevant briefings in these teams that were applicable at the time of the complaint and there were no briefings which directly or indirectly required representatives to make more than 3 unsolicited calls per year or 5 unsolicited calls per year as alleged.

Leo stated that its standard operating procedure (SOP) Interactions by Sales with HCPs set out expectations and requirements for interactions between representatives and health professionals. Within a section about face-to-face interactions, a bullet point referred specifically to the frequency, timings and duration of calls. The SOP explicitly specified that the representative should not exceed 3 calls on average and outlined what constituted a solicited call and therefore not in the scope of the 3 unsolicited calls. In addition, all representatives had to undertake annual, online refresher training on the Code which covered the requirements of the Code with respect to frequency and manner of calls and were required to pass the associated evaluation test.

**Topical dermatology department briefing**

Leo submitted that the 'customer segmentation plan' was presented to the dermatology representatives at a meeting in January 2019. The representatives were asked to aim for an annual contact (frequency) rate of 3-5 on health professionals in certain segments. A contact was any interaction with a customer, whether in the course of a solicited or unsolicited one-to-one call, or in the course of undertaking other routine activities such as attendance at an educational meeting which were attended by multiple health professionals. Such group meetings might have been organised by Leo or they might have been third party meetings (at which other companies might have been present). Interactions (contacts) at such meetings occurred by virtue of the fact that health professionals and representatives were both present at the same meeting to participate in that event and not because the representative had arranged a one-to-one solicited or unsolicited call. The maximum annual contact rate of 5 (in one health professional segment) that had been asked of the representatives was a modest target that could be comfortably achieved without exceeding 3 unsolicited calls per year.

Leo stated that the representatives were incentivised to achieve these annual contact rates, as set out in a follow-up email to them. This email set out the requirements of the Code regarding the frequency of unsolicited calls at the bottom (this requirement of the Code had also been verbally emphasised at the preceding meeting). The incentives applied to achievement of coverage (percentage of target health professionals who had received a contact) and

contact frequencies with those health professionals in each cycle (a 4-month period) were pro-rated from the annual target of contacts as set out in the earlier briefing. The amounts of incentive were modest and the maximum could be earned by achieving the specified annual contact rate (up to 5 in one of the health professional segments). Going above this rate did not qualify for additional incentive, rather the incentives were designed to effectively dis-incentivise a higher contact rate per health professional than that specified because over-calling on some health professionals would reduce the time they had to deliver the right frequency and coverage on the target health professionals. The scheme had been so designed to ensure the quality of the planned calls as much as their quantity.

No briefings were presented that required more than 3 unsolicited calls per year. Given that even the maximum annual target of 5 contacts was modest and realistic and that the associated incentives were modest (and designed to limit contact frequency to that specified), and given that the representatives had been instructed on the requirements of the Code in relation to call frequency, Leo rejected the allegation that representatives had been encouraged (whether directly or indirectly) to undertake more than 3 unsolicited calls per year. Therefore, Leo submitted that there had been no breach of the Code. Leo stated that the complainant referred specifically to 5 [unsolicited] calls and the topical dermatology briefing was the only one which had any specific reference to the number 5. Therefore, as far as it was possible to reasonably discern, the above was the only briefing that was of concern and in scope. However, it provided overview of the relevant field force briefings in the other business units:

**Bio-dermatology briefing**

Leo submitted that no briefings required representatives to undertake more than 3 unsolicited calls per year or 5 unsolicited calls per year as alleged. In fact, no formal contacts/coverage/ frequency rates had been finalised, agreed or instructed to the representatives.

**Thrombosis Briefing**

Leo submitted that the target rates had been consistent in the thrombosis business for at least 4 years. The operational metrics included the contact rate of 7 and 3.5 on target was a daily rate which sets an expectation of contacts with 7 individual health professionals, with an average of 3.5 of these being on target.

Under the customer segmentation plan which had been in place for 4 years the representatives were asked to aim for an annual contact (frequency) rate of 6 on health professionals in certain segments.

Within all representatives' annual objective setting documents, the following operational metrics for 2019 were included:

> 'Coverage of targets >90%
> Contact rate 7 and 3.5 on target
> In line with the ABPI Code of Practice Clause 15.4 on frequency of calls, no more than 3 unsolicited calls'

No briefings were presented that required more than 3 unsolicited calls per year. Leo noted that the wording 'In line with the ABPI Code of Practice Clause 15.4 on frequency of calls, no more than 3 unsolicited calls' was included in individual objective setting documentation, which showed that representatives were reminded of Code requirements about calls and were not incentivised to breach the Code.

Leo stated that the targets set, as described above, were realistic, achievable and would not require representatives to undertake more than 3 unsolicited calls per year. Therefore, Leo rejected the allegation that representatives were being encouraged to undertake more than 3 unsolicited calls per year.

For all three teams, to accurately monitor this out in the field, the CRM system included the mandatory completion of 'call classification' when inputting data into the system. This field required the representative to select 'solicited' or 'unsolicited' before the call could be submitted and finalised in the system. Across all three business units in 2018, details of the number of the representatives' records for unsolicited calls on unique health professionals were provided. Each health professional received on average 1.85 unsolicited calls from representatives. Leo submitted that this was well within the limits prescribed by the Code. In summary, Leo submitted that no business unit had encouraged representatives to exceed the number of permissible unsolicited calls per year and data from the CRM system indicated that the average number of such calls in 2018 was within the limits. Therefore, Leo denied that there had been a breach of the Code.

**2 Audits**

Leo noted that the complainant had not referred to any specific audits or related documents/evidence and had not defined what he/she meant by audit. The term audit might apply to a wide range of different activities including, but not limited to, therapy review services and scientific data generation activities. The complainant had not stated which of these he/she intended to be considered. Leo stated that it had not included scientific data generation activities or grants supplied in response to unsolicited requests.

Leo stated that across all of the business units it was not currently undertaking any active audits and it no longer offered any new services. Within the past 12 months, it had two projects which had been active but were discontinued in 2018. Details were provided.

One of the audits was the provision of written instructions and/or importable software searches for patient's identification by GPs within their practice databases for the project which ended in 2018. Leo stated that this project was undertaken as a promotional activity and was not a medical education, goods or service (MEGS) in scope of

Causes 19.1 and 19.2. The content was certified in accordance with the requirements for promotional material and briefed accordingly to representatives. It was routine practice for representatives to ask health professionals to identify patients who might be suitable for their promoted products (but to have no knowledge of, or involvement in, the management of such patients).

Therefore, Leo submitted that this project was not in scope of, nor in breach of, Clauses 19.1 or 19.2 and therefore it was not in breach of Clauses 9.1 or 2.

Leo submitted that the second audit was a third-party vendor which delivered a software programme, the Thrombosis Audit tool, and subsequent software maintenance support to various NHS hospitals.

It was several years since this software had been provided to any hospital, and in recent years support was provided to Leo primarily in the form of software maintenance; the third party could provide technical support to the hospital on the programme, if required.

In 2018, Leo identified that two trusts still used the software; details were provided.

This support was provided as a MEGS, within the scope of Clause 19.1 and 19.2. The support was provided to the NHS (and not an individual), the software tool was unbranded, and the provision was not linked to prescription, supply, administration, recommendation or purchase of a Leo medicine.

Support for the Thrombosis Audit tool stopped in 2018.

In summary, Leo submitted that neither of the identified projects were in breach of 19.1 and 19.2 and therefore were not in breach of 9.1 or 2.

**3 Speaker slides**

Leo stated that the Code required the certification of promotional speaker slides, and the applicable processes at Leo were designed to ensure that this was undertaken.

Leo submitted that the complainant had not made it clear as to which speaker slides or types of meetings were at issue. Given the breadth of this complaint and the sparse information, Leo provided a copy of its SOPs about meetings and the certification process. The SOP gave detailed definitions of meetings and the required process for their approval. The meeting approval process was completed in the CRM system. The SOP clearly outlined that if the meeting was promotional, all relevant content had to be approved through the internal approval process.

Since September 2018, in addition to this SOP, control had been implemented (which had not yet been incorporated into the SOP but had been trained to the representatives) with the inclusion of a 'HCP compliance' approval step ('HCP compliance' consisted of a senior compliance executive or medical manager). This requirement was described in a guidance document and the associated approval flow was embedded in the CRM system which the representatives must use.

Leo stated that the electronic review process was outlined in a working instruction. Within this was stated the process review, approval and certification of material and a clear description of the internal process to be followed including individual roles and responsibilities and the system used was given.

Veeva PromoMats acted as internal monitoring to show whether promotional speaker slides had been certified/approved to the originator of the job bag and as part of his/her responsibilities the process required him/her to communicate this to the job bag owner and approve the document for distribution, as outlined in the SOP. Leo maintained a list of nominated medical signatories and non-medical/ other signatories as required by Clause 14.1.

Furthermore, in Leo's speaker agreement and briefing letter, the section 'Presentation Requirements' specifically instructed the speaker to ensure that his/her slides were submitted to the meeting organiser at least 10 days before the event. This additional control measure was intended to prevent unapproved/uncertified promotional slides from potentially being used.

In summary, Leo stated that the processes as described required promotional speaker slides to be certified. Therefore, Leo denied a breach of Clause 14.1 and 9.1.

**4 Adverse event reporting**

Leo submitted that it took compliance with pharmacovigilance (PV) requirements very seriously. This included compliance with reporting adverse events (AEs), other experiences (OEs) and product complaints (PCs) and training all employees including representatives. The Leo Code of Conduct was mandated by the Global Safety department and stipulated that all Leo employees were trained when they started employment with the company and annually thereafter.

Leo submitted that in the UK, all new employees (and those returning from long term sick or maternity leave) were trained and instructed in detail on PV knowledge and reporting requirements as part of core induction training, as set out in a working instruction. All field force members undertook PV training which included PV training presentations, as well as scenario testing pertinent to the relevant therapeutic area, before they were allowed to promote Leo products. Examples of field based initial training were provided. This training covered all elements of PV including its history, why it was needed, how it was regulated, the role of the Qualified Person in Pharmacovigilance (QPPV) and UK Safety Contact person (SCP) who were available 24/7, classification of AE/OE/PCs, social media usage, out of office requirements and the Leo reporting requirements, timeframes and method of reporting via email or telephone to Leo medical information. The PV training clearly set out the expectations

to report all AEs, OEs and PCs even if it was an expected event documented in the SPC for any Leo product.

Attendance sheets were completed for each training and signed by the PV trainer. Copies of the slides used together with the attendance sheets and quizzes were maintained electronically and in hard copy. PV training was tracked on a PV tracker maintained electronically in a secure folder. In addition, staff kept a note of PV training in their own training records. All staff were issued with a pocket-sized card which contained reminder instructions on AE reporting that covered all the details for reporting and important definitions.

Annual PV training was conducted face-to-face or via skype to all staff including the field force; the training was adapted to reflect new information and was tailor-made each year to maintain engagement, it contained all core elements of PV together with reporting requirements and scenario testing quizzes. Attendance sheets were completed. All annual training was tracked and filed appropriately. Assessment of the quality of training was conducted.

Leo firmly rejected the allegation that it encouraged representatives not to report adverse reactions. On the contrary, Leo undertook mandatory induction and annual training for all staff and therefore Leo submitted that there had been no breach of Clauses 15.6, 15.9, 9.1 or 2.

**5 Emails to customers**

Leo noted that the complainant had not referred to a specific email sent without prior consent from a recipient health professional nor of any associated briefings and nor had he/she provided any relevant evidence. Leo stated that it would focus on describing its processes for the issuing of promotional emails by the field force that required prior consent from the recipient health professional. The company stated that its process prevented any promotional emails from being distributed without explicit and documented prior opt-in consent for receipt of promotional information.

Within the SOP Interactions by Sales with HCPs there were several points outlined about emailing customers. This SOP clearly stated that email might not be used for promotional purposes without the explicit and documented consent of the recipient.

Details for each of the three therapy teams were provided.

Leo stated that in summary, it was not possible for a representative in any of the business units to send an approved promotional email outside of the CRM system. The system itself would not send an email without a documented and signed opt-in prior consent from the intended recipient.

Leo submitted that there were no briefings and instructions from the company which encouraged representatives to email customers without their permission. On the contrary, representatives had been briefed on the compliant manner for securing consent before sending promotional emails and had made such approved promotional emails available only in the electronic CRM system within which it was impossible to send such emails without documented prior consent. Leo thus denied a breach of Clauses 9.1 and 9.9.

**Conclusion**

Leo stated that, as demonstrated, it had a range of detailed procedures and training to ensure compliance with the Code. This included procedures and training for the activities referred to by the complainant. The company's investigation did not find any instances of briefings that encouraged representatives to breach the Code in relation to unsolicited call rates, audits, promotional speaker slides, email consents or adverse event reporting. On the contrary Leo noted that it had provided procedural documents and briefings which demonstrated compliance.

Leo stated that it took compliance to the Code very seriously and that it rejected any breach of Clauses 2, 9.1, 9.9, 14.1, 15.6, 15.9, 19.1 and 19.2.

**PANEL RULING**

The Panel noted that the complainant only provided brief details about his/her complaint. There were no attachments provided to support the allegations. A complainant had the burden of proving his/her complaint on the balance of probabilities. The Panel noted the detailed response from Leo. It considered each allegation as follows:

**1 Visits to doctors**

The Panel noted that the supplementary information to Clause 15.4 stated, *inter alia*, that the number of calls made on a doctor or other prescriber by a representative each year should not normally exceed three on average. This did not include attendance at group meetings and such like, a visit requested by the doctor or other prescriber or a visit to follow up a report of an adverse reaction, all of which could be additional to the three visits allowed.

The supplementary information also included that when briefing representatives, companies should distinguish clearly between expected call rates and expected contact rates. Contacts include those at group meetings, visits requested by doctors or other prescribers, visits in response to specific enquiries and visits to follow up adverse reaction reports. Targets must be realistic and not such that representatives breach the Code in order to meet them.

The Panel noted Leo's submission that a customer segmentation plan for the topical dermatology business unit presented at an internal meeting in January 2019 asked representatives to aim for an annual contact rate of 3-5 for health professionals in certain segments. The Panel further noted Leo's submission that the maximum annual contact rate of 5 could be comfortably achieved without exceeding 3 unsolicited calls per year as it defined a 'contact' as any interaction with a customer and

included, *inter alia*, attendance at group meetings. The Panel noted that the slides from the customer segmentation plan in question referred to 'calls' not 'contacts' and made no reference to the Code or the supplementary information. The Panel noted Leo's submission that the Code requirements were verbally noted at the meeting in question. A follow-up email to the representatives described the financial incentives available if targets were achieved and included the statement: 'Please be aware that in line with the ABPI code of practice you cannot conduct more than 3 unsolicited calls on a customer in a 12 month period. If the calls are solicited there is no limit'. There was no definition for what constituted a solicited call. The Panel noted that Leo's SOP on interactions by sales with health professionals stated that the number of calls made upon a doctor or other prescriber by a representative each year should not exceed three on average and it outlined examples of activities which could be in addition to those three calls.

With regard to another business unit, bio-dermatology, the Panel noted Leo's submission that no formal contacts/coverage/frequency rates had been finalised, agreed or instructed to the representatives and targets for 2019 were to be determined in individual plans of action.

With regard to the thrombosis business unit, the Panel noted Leo's submission that representatives were asked to aim for an annual contact rate of 6 for health professionals in certain customer segments. The Panel noted that the thrombosis customer segmentation plan slides submitted by Leo made no reference to target annual call or contact rates and the company had provided the Authority with no material that referred to this annual contact rate of 6.

The Panel noted Leo's submission that across all three business units in 2018, analysis of the customer relationship manager system indicated that each individual health professional received on average 1.85 unsolicited calls from Leo.

The Panel considered that there was no evidence before it that the actual number of calls made on a doctor or other prescriber by a representative had breached the requirements of the Code. However, the Panel was concerned about the representative briefing material. The Panel noted that Clause 15.9 stated that briefing material for representatives must not advocate, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code. The detailed briefing material referred to in this clause consisted of both the training material used to instruct representatives about a medicine and the instructions given to them as to how the product should be promoted.

The Panel noted that the topical dermatology customer segmentation plan slides which referred to call frequency did not differentiate between an unsolicited call and a 'contact' as defined by Leo and made no reference to the Code requirements. The Panel considered that the slides should have clearly set out the position. Although it was helpful to remind representatives of the Code requirements verbally, in a follow-up email and in the SOP, in the Panel's view, each representative briefing that related to call frequency needed to stand alone and should have reiterated the Code requirements and definitions of a call versus a 'contact' as defined by Leo. It was important to be clear particularly as representatives were rewarded for certain call/contact related activities.
Noting its comments above, the Panel considered that the reference to call frequencies of 4 and 5 for health professionals in the topical dermatology customer segmentation slides, without any definition of a call or reiteration of the Code requirements, meant that, on the balance of probabilities, the briefing material advocated a course of action likely to lead to a breach of the Code and the Panel ruled a breach of Clause 15.9. On balance, the Panel did not consider, given the particular circumstances of this case, that Leo had failed to maintain high standards in this regard and ruled no breach of Clause 9.1.

**2 Audits**

The Panel noted Leo's submission that it was not currently undertaking any audits but had two projects in the past 12 months which had now been discontinued. The first project was a set of written search instructions and/or importable software searches, developed by a third party, which were intended to help GPs identify patients suitable for Enstilar within the practice database; Leo submitted that this was not a medical and educational goods or services (MEGS) arrangement but a promotional activity. The second project Leo submitted was a MEGS and support was provided to NHS trusts in the form of a software tool to capture cases of venous thromboembolism and to run reports on such cases in order to identify trends within the hospital; the data was not shared with nor utilised by Leo and the provision of the MEGS was not linked to the prescription, supply, administration, recommendation or purchase of a Leo medicine.

The Panel considered that the complainant's allegation was unclear with regard to which audit(s) he/she was referring to. It was not for the Panel to infer detailed reasons to support allegations. Complainants needed to provide sufficient detail so that the respondent company and the Panel could clearly understand the concerns. Further it was for the complainant to establish his/her case on the balance of probabilities. It was not necessarily a breach of the Code for audits to be linked to the use of a medicine; all the relevant circumstances would need to be considered. The Panel considered that the very general nature of the allegation and the lack of evidence was such that the complainant had not discharged his/her burden of proof. The Panel therefore ruled no breach of Clauses 19.1 and 19.2 and thus no breach of Clauses 9.1 and 2 in this regard.

**3 Speaker slides**

The Panel noted that the complainant had not referred to any specific speaker slides. The Panel noted Leo's submission that its processes require

promotional speaker slides to be certified. The Panel noted that the LEO SOP 'Medical Events – Meetings, LEO organised and LEO sponsored UK/IE' included in relation to certification requirements:

> 'All meetings in the scope of this SOP require the following documentation to have been approved within ERACs [electronic review approval and certification system]…If pre-approved templates are not used, the following materials used for promotional materials, will be subject to certification: Speaker slides – for promotional meetings only.'

The Panel further noted Leo's submission that its speaker agreement and briefing letter instructed speakers to submit their slides to the meeting organiser at least 10 days before the event and that this was to prevent uncertified slides from being used.

The Panel considered that, based on the evidence before it, the complainant had not proved, on the balance of probabilities, that speaker slides had not been appropriately approved as required by the Code. The Panel thus ruled no breach of Clauses 14.1 and 9.1 in this regard.

**4 Adverse event reporting**

The Panel noted Leo's submission that all field force staff undertook pharmacovigilance training, which included presentations and relevant therapy area scenario testing, prior to commencing promotional activities and annual pharmacovigilance training was conducted for all staff including the field force. The Panel further noted Leo's submission that the training clearly laid out the expectation to report all adverse events, other experiences and product complaints for all Leo medicines, even if it was an expected event documented in the summary of product characteristics (SPC).

The Panel noted that Clause 15.6 of the Code stated that representatives must transmit forthwith to the scientific service referred to in Clause 25.1 any information which they receive in relation to the use of the medicines which they promote, particularly reports of adverse reactions. The Panel noted that it was of the utmost importance that information about adverse reactions and such like was processed by the company in accordance with, *inter alia*, the Code.

The Panel noted that the complainant had provided no evidence in support of his/her allegation that the field force was encouraged not to report adverse reactions. The Panel considered that, based on the evidence before it, the complainant had not proved, on the balance of probabilities, that there had been a breach of the Code in this regard. The Panel therefore ruled no breach of Clauses 15.6, 15.9, 9.1 and 2.

**5 Emails to customers**

The Panel noted that the complainant had not referred to any specific instances or provided any evidence in support of his/her allegation that representatives were encouraged to email customers without their permission. The Panel noted that Leo's SOP 'Interactions by Sales with HCPs [healthcare professionals] UK/IE' stated: '… telephone, text messages and email must not be used for promotional purposes except with the prior permission of the recipient'. The Panel further noted Leo's submission that it was not possible for a representative in any of the business units to send a Leo approved promotional email outside of the customer relationship management system and that the system itself would not issue an email without documented prior consent for the receipt of promotional information.

The Panel considered that, based on the evidence before it, the complainant had not proved, on the balance of probabilities, that representatives were encouraged to email customers without their permission. The Panel therefore ruled no breach of Clause 9.9 and no breach of Clause 9.1 in this regard.

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|---|---|
| **Complaint received** | **19 February 2019** |
| **Case completed** | **18 June 2019** |

# COMPLAINANT v ASTRAZENECA

## Use of Twitter

**A complainant who described him/herself as a concerned UK health professional complained about a re-tweet by AstraZeneca which alerted readers to the fact that, during heart failure awareness week, the company had joined the Heart Failure Society of America to help raise awareness of heart failure and its prevention.**

**The complainant noted that the tweet, initially sent out by AstraZeneca in the US, had been re-tweeted by AstraZeneca in the UK; he/she was concerned that the material would not have been properly processed in the UK and that it would have been seen by members of the public. The complainant noted that the tweet had several links from what was AstraZeneca's space to other uncontrolled facets of Twitter as well as other websites.**

**The detailed response from AstraZeneca is given below.**

**The Panel noted that the original US tweet was re-tweeted from AstraZeneca's global twitter account. The global headquarters was based in the UK and thus the global twitter account and the re-tweet had to comply with the UK Code.**

**The Panel noted that the tweet highlighted a disease awareness week and included a link to the schedule of events. The Panel noted AstraZeneca's submission that the re-tweet was non-promotional in nature and neither it, nor the linked events schedule, mentioned any specific medicine. The Panel ruled no breach of the Code as the re-tweet had been certified as a non-promotional item prior to being issued.**

**The Panel noted that the complainant had provided no evidence that AstraZeneca had failed to provide adequate training with regard to the release of the tweet and therefore, based on the narrow allegation, no breach of the Code was ruled.**

**The Panel noted that the 2016 Code stated that it should be made clear when a user was leaving any of the company's sites, or sites sponsored by the company, or was being directed to a site which was not that of the company. In the Panel's view, it was clear that the link took the reader to the Heart Failure Society of America's webpage for Heart Failure Awareness Week 2019. The Panel therefore ruled no breach of the Code.**

**The Panel noted that there was no evidence that AstraZeneca had failed to maintain high standards and no breach of the Code was ruled in that regard.**

A complainant who described him/herself as a concerned UK health professional complained about a re-tweet by AstraZeneca. The tweet read:

'This Heart Failure Awareness Week, we're joining @HFSA [Heart Failure Society of America] to help raise awareness of #heartfailure and prevention. Check out the #HFWeek2019 schedule of events to learn more spr.ly/6010EruFM. #AmericanHeartMonth.'

Below this text was artwork promoting HFSA and the heart failure week. There was a strapline 'Do your part, know your heart'.

**COMPLAINT**

The complainant noted that although the tweet was initially sent out by AstraZeneca in the US, it had been re-tweeted by AstraZeneca in the UK. The complainant was concerned that the material would not have been properly processed in the UK. Clearly the tweet was available to everyone including the public.

The complainant noted that the tweet had several links by various methods (@, # and compressed links). These were links from what was AstraZeneca's space to other uncontrolled facets of Twitter as well as other websites. The complainant alleged breaches of Clauses 9.1, 14.3, 14.5 (since it was covered by 14.3), 16.1 (with adequate training this would not be released) and 28.6 of the [2016] Code.

**RESPONSE**

AstraZeneca submitted that neither the original tweet nor re-tweet were promotional; they were issued as standard, non-promotional tweets to promote disease awareness of heart failure to a US and global audience.

AstraZeneca noted that the two tweets were issued on two twitter handles operated by two distinct legal entities of AstraZeneca. The first tweet was issued on the Twitter handle '@AstraZenecaUS' which was operated by and registered to AstraZeneca US. AstraZeneca US was headquartered in Wilmington, Delaware and was the legal entity responsible for AstraZeneca's North American operations. The second tweet was a re-tweet of the first issued on the handle '@AstraZeneca' which was operated by and registered to AstraZeneca PLC. AstraZeneca PLC was located in Cambridge, UK and was the global headquarters for the AstraZeneca group of companies. Being domiciled in the UK, the actions of AstraZeneca PLC and its employees were subject to the Code where applicable.

AstraZeneca noted that the complaint did not involve AstraZeneca UK which operated the Twitter handle '@AstraZeneca UK' and was responsible for AstraZeneca's operations in the UK.
Both tweets focused on the US Heart Failure Awareness Week 2019 (10-16 February 2019). The

awareness week was created by the HFSA by a declaration through the US senate in 2001. HFSA Inc. was conceived in 1995 by a small group of academic cardiologists and aimed to bring health professionals, including researchers, physicians and nurses together to learn more about the mechanisms of the disease, how best to treat patients, play a role in reducing health care costs, etc.

AstraZeneca submitted that the subject matter of the two tweets was appropriate for both a US and global audience because

a) Heart failure was a global pandemic which affected at least 26 million people worldwide and was increasing in prevalence. In the US alone, there were 5.7 million adults diagnosed with heart failure. This represented healthcare costs of over $30 billion. Despite this significant health burden, HFSA represented the first organised effort by heart failure experts from the Americas to provide a forum for all those interested in heart function, heart failure, and congestive heart failure (CHF) research and patient care; this made the organisation and its disease awareness efforts of global relevance.

b) Heart failure was a key therapeutic area of focus for AstraZeneca, and the company was committed to increasing awareness of this disease, improving clinical pathways through collaborations and developing new medicines to treat and prevent the disease.

c) The non-promotional tweets did not pertain to any medicine marketed by AstraZeneca.

Given the global relevance of increasing heart failure awareness, the hashtags used in the tweets (#heartfailure, #HFweek2019, #AmericanHeartMonth) were relevant to global and US audiences as they referenced the disease and relevant awareness events. In addition, the hashtags used were not directly linked with any AstraZeneca medicine(s).

The short link provided (http://spr.ly/6010EruFM) in the tweets pointed to the HFSA's webpage for Heart Failure Awareness Week 2019. The webpage mainly featured events that were accessible to a global and US audience (tweet chats, webinars, etc), that focused on awareness and education around the topic of heart failure and were therefore relevant to both a global and US audience. There was no link or mention of AstraZeneca medicines on this webpage. AstraZeneca was not involved in the creation of the webpage and it did not influence or review any of the activities listed on the webpage as part of the awareness week. When readers clicked on the link it was made evident to them that they had entered an HFSA webpage. Key indicators included the web address that appeared at the top of the browser window and the HFSA logo at the start of the webpage.

AstraZeneca disputed the need for a 'pop up warning' for readers that clicked on to the link because of the unambiguous nature of the webpage serviced by the short link and the link appeared on a tweet and not a website. AstraZeneca denied a breach of Clause 28.6.

AstraZeneca submitted that the content of the tweet was created and published in adherence with all relevant internal procedures. The second tweet was approved in adherence with AstraZeneca PLC's relevant standard operating procedure (SOP). The SOP had been written to meet the rigorous standards of the Code. The re-tweet was approved and certified as a non-promotional item (it met the requirements of Clauses 14.3 and 14.5) on 12 February 2019 by an MHRA and PMCPA medical registered signatory who was a UK registered pharmacist (this met the requirements of Clause 16.1). The tweet was issued on 13 February 2019. AstraZeneca provided a timeline for approval and the process followed. Therefore, the link and the webpage had been assessed by the signatory certifying this re-tweet in keeping with internal processes and procedures.

In conclusion, AstraZeneca denied breaches of Clauses 14.3, 14.5, 16.1 and 28.6 of the Code. Further, the company submitted that it had maintained the highest standards when approaching this activity and it denied a breach of Clause 9.1.

**PANEL RULING**

The Panel noted that the use of social media including twitter to provide information to the public was a legitimate activity as long as the material complied with the Code.

The Panel noted that the original tweet was sent by AstraZeneca US from the US twitter account and was re-tweeted from AstraZeneca's global twitter account. The global headquarters was based in the UK and thus the global twitter account and the re-tweet had to comply with the UK Code.

The Panel noted that the tweet highlighted the United States' Heart Failure Awareness Week 2019 being run by the Heart Failure Society of America and included a link to the schedule of events. The Panel noted AstraZeneca's submission that the re-tweet was non-promotional in nature and neither it nor the linked events schedule mentioned any specific medicine.

Clause 14.3 stated that educational material for the public or patients which related to diseases or medicines had to be certified in advance. Clause 14.5 stated that the certificate for material covered by Clause 14.3 must certify that the signatory has looked at the final form of the material to ensure that in his/her belief it complied with the Code. The Panel noted that the re-tweet had been certified as a non-promotional item prior to being issued and therefore the Panel ruled no breach of Clauses 14.3 and 14.5.

With regard to the alleged breach of Clause 16.1, the Panel noted that the complainant had provided no evidence that AstraZeneca had failed to provide adequate training with regard to the release of the tweet and therefore, based on the narrow allegation, no breach of Clause 16.1 was ruled.
The Panel noted that Clause 28.6 of the 2016 Code stated that it should be made clear when a user was leaving any of the company's sites, or sites sponsored by the company, or was being directed to a site which was not that of the company. In the

Panel's view, it was clear that the link took the reader to the Heart Failure Society of America's webpage for Heart Failure Awareness Week 2019. The Panel therefore ruled no breach of Clause 28.6. In relation to AstraZeneca's submission that the link appeared within a tweet and not on a website, as referred to in Clause 28.6, the Panel noted that this was correct for the 2016 Code but the changes to Clause 28 in the 2019 Code would be relevant in future.

The Panel noted that there was no evidence that AstraZeneca had failed to maintain high standards and no breach of Clause 9.1 was ruled.

**Complaint received** **19 February 2019**

**Case completed** **9 May 2019**

# COMPLAINANT v MERCK SHARP & DOHME

## Alleged frequent and disguised promotional emails

**A complainant who described him/herself as a concerned UK health professional, complained about two almost identical emails from Merck Sharp & Dohme, received within minutes of each other. The emails were headed 'Explore MSD Connect Today' and invited recipients to access the latest information about Merck Sharp & Dohme products, support their patients with online resources and sign-up for online and live events.**

**The complainant noted that the two emails had different subject lines ('Diabetes 101 – what's new?' and 'Diabetes Round-up') neither of which indicated that the content was promotional. The complainant noted that he/she had signed up to receive emails but considered that two identical emails in half an hour was excessive especially as it was not clear that each email was a signpost to a promotional website. Finally, the complainant noted that there did not appear to be a link to prescribing information for any product on the website.**

**The detailed response from Merck Sharp & Dohme is given below.**

**The Panel noted there was no direct or implied mention of any medicine in the emails at issue, however, both emails referred to and included links to a promotional website. In the Panel's view, recipients would be clear that the MSD Connect website would include information about the company's medicines as stated in the content of the email. However, the Panel considered that as the emails did not promote any specific medicines, the emails were not in themselves promotional and therefore were not disguised. There was no need to include prescribing information. No breaches of the Code were ruled.**

**The Panel noted Merck Sharp & Dohme's submission that when a reader accessed the MSD Connect website, prescribing information was clearly available. The Panel noted that the complainant bore the burden of proof and did not consider that he/she had provided evidence to show that, on the balance of probabilities, the MSD Connect website did not include prescribing information for any of Merck Sharp & Dohme's medicines as alleged and no breach of the Code was ruled.**

**The Panel noted Merck Sharp & Dohme's submission that the two emails had been sent to the same health professional within seconds due to a technical error experienced by a third party. The same email, using different subject lines, was sent to a number of health professionals within seconds of each other. On balance, based on the particular circumstances of this case, the Panel did not consider that this meant that high standards had not been maintained. No breach of the Code was ruled.**

A complainant who described him/herself as a concerned UK health professional, complained about two almost identical emails from Merck Sharp & Dohme which he/she received within minutes of each other. The emails were headed 'Explore MSD Connect Today' and invited recipients to access the latest information about Merck Sharp & Dohme products, support their patients with online resources and sign-up for online and live events. There was a graphic related to diabetes under which it was stated 'Register with MSD Connect to access this whitepaper and additional content'. Below that statement was a boxed statement regarding the reporting of adverse events via the Yellow Card scheme and also to Merck Sharp & Dohme. Both emails had the same reference number, GB-NON-00443.

**COMPLAINT**

The complainant noted that, although identical, the two emails had different subject lines ('Diabetes 101 – what's new?' and 'Diabetes Round-up') neither of which indicated that the content was promotional. The complainant stated that, because of the different subject lines, the sending of the two emails was deliberate and not due to a technical glitch. The complainant noted that he/she had signed up to receive emails but considered that two identical emails in half an hour was excessive especially as it was not clear that each email was a signpost to a promotional website. Finally, the complainant noted that there did not appear to be a link to prescribing information for any product on the website.

When writing to Merck Sharp & Dohme, the Authority asked it to consider the requirements of Clauses 4.1, 9.1 and 12.1 of the 2016 Code.

**RESPONSE**

Merck Sharp & Dohme explained that in September 2018, it instructed a named media-buying agency to conduct A/B testing on the email in question which was intended to promote MSD Connect (a promotional website) to health professionals. This activity was then sub-contracted to the publishing house that managed a general practice journal and website, and which had significant experience in A/B testing of emails.

Merck Sharp & Dohme submitted that A/B testing was a standard marketing approach that sought to provide a tailored and personalised email experience for health professionals. In this case, Merck Sharp & Dohme set up two versions of an email, each with a different subject line (version A and version B) but with exactly the same content in each. The intention was that these would be

sent to a test group of health professionals who had previously consented to receive promotional emails. Half of the test group was to be sent version A, while the other half was to be sent version B. Metrics would then set out which version was opened the most. Based on this information, Merck Sharp & Dohme could then send that version to a wider group of health professionals who had consented to receive emails.

Merck Sharp & Dohme submitted that the A/B testing email in question was certified on 17 February 2019. The A/B testing email with the two different subject lines was sent out by the publishing house on 18 February 2019 but despite instructions, both subject headed emails were sent to the same health professionals within seconds of each other. This was not Merck Sharp & Dohme's intention and the publishing house had acknowledged that this was the consequence of a technical fault within its organisation. The sending of two emails was not what had been agreed and was not deliberate as it undermined the purpose of the A/B testing; it also exposed health professionals to the repeat/identical email content.

Once it knew of the issue, Merck Sharp & Dohme immediately halted any other A/B testing of emails until the agencies involved had taken appropriate preventative and corrective action to ensure that health professionals were not subjected to the same experience again.

Merck Sharp & Dohme noted the allegation that there did not appear to be a link to prescribing information to any product on the website. The company assumed that the complainant had commented on the email in question and not the promotional website. As the email did not contain any product name, information or claims Merck Sharp & Dohme did not consider that it fell under Clause 4.1 as it was not promotional material for a medicine. Once the website MSD Connect was reached, then prescribing information was clearly available one click away. The company denied any breach of Clause 4.1.

Merck Sharp & Dohme noted that the complainant had alleged that the emails amounted to disguised promotion. Merck Sharp & Dohme stated, however, that it was clearly indicated in email inboxes that the emails in question contained promotional information (a relevant screenshot was provided). Additionally, there was a clear header on the emails that stated 'This email has been sent by [named third party] and contains third party promotional information'. Merck Sharp & Dohme noted the complainant's acknowledgement that he/she signed up to receive promotional emails and, given the above, it considered that the emails were sufficiently clear that they contained promotional content. Furthermore, as stated in relation to Clause 4.1 above, once a health professional landed on MSD Connect, it was very clearly signposted as a promotional website, from which prescribing information, per product, was one click away. Merck Sharp & Dohme thus denied a breach of Clause 12.1.

Additionally, Merck Sharp & Dohme submitted that it was clear that the emails in question contained promotional information for a website, however, the emails themselves were not promotional for a medicine and therefore did not need to have prescribing information. Merck Sharp & Dohme denied any breach of Clause 9.1 as it did not believe it had failed to maintain high standards.

In summary, Merck Sharp & Dohme submitted that the emails created complied with the Code and were sent with the appropriate permissions in place and clearly signposted as containing promotional material. Whilst Merck Sharp & Dohme recognised that this had upset one health professional, for which the company sincerely apologised, the matter, in its view, did not amount to any breach of the Code.

**PANEL RULING**

The Panel noted the complainant's allegation that the subject line of both emails did not indicate that the content of either email was promotional. The Panel noted that there was no direct or implied mention of any medicine in the emails at issue, however, both emails referred to and included links to a promotional website. In the Panel's view, recipients would be clear that the MSD Connect website, that was being introduced to readers within the emails, would include information about Merck Sharp & Dohme's medicines as stated in the content of the email. However, the Panel considered that as the emails did not promote any specific Merck Sharp & Dohme medicines, the emails were not in themselves promotional and therefore were not disguised. The Panel therefore ruled no breach of Clause 12.1.

The Panel noted Merck Sharp & Dohme's submission that when a reader accessed the MSD Connect website, prescribing information was clearly available one click away. Merck Sharp & Dohme provided an example of a webpage with links to the prescribing information appearing at the bottom of the page. The Panel did not review the entire MSD Connect website. The Panel noted that the complainant bore the burden of proof and did not consider that he/she had provided evidence to show that, on the balance of probabilities, the MSD Connect website did not include prescribing information for any of Merck Sharp & Dohme's medicines as alleged and no breach of Clause 4.1 was ruled in relation to the MSD Connect website.

The Panel noted its comments above and considered that as the emails at issue did not promote any specific Merck Sharp & Dohme medicines, there was no requirement to include prescribing information in the emails. The Panel therefore ruled no breach of Clause 4.1 in relation to each email.

The Panel noted that the complainant stated that he/she had signed up to receive emails. The supplementary information to Clause 9.9 ensured that emails included information as to how to unsubscribe from receiving them. The Panel noted

Merck Sharp & Dohme's submission that the two emails with different subject lines had been sent to the same health professional within seconds due to a technical error. This was unfortunate and Merck Sharp & Dohme had been let down as a result of a technical error experienced by a third party agent for which it was, nonetheless, responsible for under the Code. The same email, using different subject lines, was sent to a number of health professionals within seconds of each other. On balance, based on the particular circumstances of this case, the Panel did not consider that this meant that high standards had not been maintained. The Panel therefore ruled no breach of Clause 9.1.

**Complaint received** **18 February 2019**

**Case completed** **28 May 2019**

# GILEAD SCIENCES v VIIV HEALTHCARE

## Promotion of Tivicay and Juluca

**Gilead Sciences Europe complained about materials being used by ViiV Healthcare to promote Tivicay (dolutegravir) and Juluca (dolutegravir/rilpivirine).**

**The detailed response from ViiV is given below.**

**1 Alleged off-label promotion of Tivicay**

**Gilead stated that during the HIV Drug Therapy conference held in Glasgow, 28-31 October 2018, ViiV promoted results from the GEMINI-1 and GEMINI-2 studies which investigated the efficacy and safety of dolutegravir (DTG) in combination with one other antiretroviral (ARV) agent, lamivudine (3TC), for the treatment of HIV in treatment naïve patients and alleged that this was not in accordance with the marketing authorization and was inconsistent with the SPC for Tivicay at that time.**

**Gilead did not refer to specific materials but provided photographs of exhibition panels which it sated were 'some examples'. The Panel therefore considered the allegation in general and not in the context of any specific materials.**

**The Panel noted that the indication in Section 4.1 of the Tivicay SPC stated:**

> **'Tivicay is indicated in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV) infected adults, adolescents and children above 6 years of age'.**

**The Panel noted that the indication in Section 4.1 did not specify a minimum or a maximum number of ARV medicines that Tivicay should be combined with. Section 4.2 (posology and method of administration) stated that Tivicay should be prescribed by physicians experienced in the management of HIV infection. Section 5.1 (pharmacodynamic properties) referred to various combinations of DTG with other ARV medicines including 3TC.**

**The Panel noted Gilead's assertation that at the time Tivicay was granted a marketing authorization for the above indication, no data existed on the use of DTG in combination with one other ARV agent in HIV treatment naïve patients.**

**The Panel noted that at the time of the conference, the Tivicay SPC did not refer to the GEMINI studies. According to ViiV, following the conference, in November 2018, the SPC was updated to include, *inter alia*, GEMINI-1 and GEMINI-2 study results in Section 5.1 and information based on these studies was included in Section 4.4 (special warnings and precautions for use) which stated:**

> **'Lamivudine and dolutegravir**
> **The two-drug regimen of dolutegravir 50 mg once daily and lamivudine 300 mg once daily was explored in two large randomized and blinded studies, GEMINI 1 and GEMINI 2 (see section 5.1). This regimen is only suitable for the treatment of HIV-1 infection where there is no known or suspected resistance to the integrase inhibitor class, or to lamivudine'.**

**In the Panel's view it was not necessarily unacceptable to promote a medicine using studies that were not listed in its SPC as long as such data was not inconsistent with the particulars listed in the SPC. In the Panel's view, using Tivicay in combination with one other ARV medicine in HIV was not in itself inconsistent with the indication for Tivicay to be used in combination. Physicians might decide not to use a two drug-regimen prior to the availability of data.**

**The Panel noted its comments above and considered that Gilead had not proved, on the balance of probabilities, that ViiV's promotion of Tivicay in combination with lamivudine at the October 2018 conference in general, constituted promotion of Tivicay outside the terms of its marketing authorization or in a manner that was inconsistent with its SPC. No breach of the Code was ruled. The Panel did not consider that ViiV had failed to maintain high standards and ruled no breach of the Code.**

**Clause 2 was a sign of particular censure and was reserved for such use. The Panel noted its rulings of no breach above and consequently ruled no breach of Clause 2.**

**2 Alleged use of Tivicay data in combination with two antiretroviral agents to support promotion of Tivicay with one antiretroviral agent**

**Gilead alleged that the claim 'Only dolutegravir has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens', available on the UK ViiV Exchange website, when used in the context of the promotion of two drug regimens, was misleading and incapable of substantiation.**

**Gilead also alleged that the claim 'Unbeaten in head to head clinical trials', made at the ViiV stand during the Glasgow HIV conference, was ambiguous, misleading, gave the impression that the attributes of DTG seen in triple therapy studies were also delivered when DTG was used as part of a two-drug regimen, and did not compare medicines for the same needs or intended for the same purpose.**

**The Panel noted that item VIIV/DTGRPV/0033/18(3) was a webpage on the ViiV exchange website with a focus on 2-drug regimens. The webpage included the subheading 'What makes DTG an ideal core agent to power a 2DR [2-drug regimen]?'. Below this, in smaller font, it stated 'Only dolutegravir…' followed by a number of claims including: 'Has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens'; and 'Is PROVEN EFFECTIVE in 2-drug regimens with lamivudine in treatment-naïve adult patients at 48 weeks and rilpivirine in virologically suppressed patients at 100 weeks'. 'SUPERIOR EFFICACY' and 'PROVEN EFFECTIVE' in the above two claims were in a different coloured font to the surrounding text.**

**The Panel noted that below this section of the webpage was a 'learn more' section which stated 'Explore dolutegravir-based, 2-drug regimens for your diverse patient needs' followed by the logos for Tivicay + lamivudine and Juluca.**

**The Panel noted that both the Tivicay and the Juluca SPCs stated that these medicines should be prescribed by physicians experienced in the management of HIV infection. The Panel considered the immediate and overall impression to an HIV physician. In the Panel's view, although the claim in question featured on a webpage promoting DTG-based 2-drug regimens, it appeared beneath the question of what made DTG an ideal core agent to power a 2-drug regimen. In the Panel's view it was clear that 'SUPERIOR EFFICACY' in the claim 'Only dolutegravir…Has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens' was in relation to DTG as a core agent in a 3-drug regimen and not in relation to a 2-drug regimen as alleged. An associated claim stated that DTG was '…PROVEN EFFECTIVE…' in two specific 2-drug regimens in certain patients. In this regard, the Panel considered that the intended audience would not be misled as alleged. Gilead had not shown, on the balance of probabilities, that the claim 'Only dolutegravir…Has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens' was misleading or incapable of substantiation as alleged and the Panel therefore ruled no breach of the Code.**

**The Panel did not consider that ViiV had failed to maintain high standards in this regard and ruled no breach of the Code.**

**The Panel noted that the claim 'Unbeaten in head to head clinical trials' appeared on an interactive ViiV stand panel at the HIV Drug Therapy 2018 conference, and directly below the claim, in smaller font, it stated 'Tap to explore the dolutegravir (DTG) data'. To the left of the heading was a circle that stated 'Powered by DTG at the core'. Below this were three large circles which were labelled: GEMINI-1 and GEMINI-2 data, SWORD-1 and SWORD-2 data, and depth and breadth of DTG clinical trials. When the circles were accessed, further information about the studies was provided, including that the GEMINI and SWORD studies were non-inferiority studies and evaluated DTG as part of a 2-drug regimen and that 10 studies, including superiority and non-inferiority studies, evaluated DTG as part of a 3-drug regimen.**

**That Panel considered that the first screen of the interactive stand panel needed to stand alone as not all individuals would stop to click through the screens and read the supporting information.**

**The Panel noted ViiV's submission that in every phase 3, head to head study that DTG had been included in, the results had either shown DTG based regimens to be superior or non-inferior in comparison with regimens based on other ARVs and that no combination of ARVs had shown superiority over a DTG-based regimen in any head-to-head clinical trial in any patient population.**

**In the Panel view, the word 'unbeaten' would imply to the audience that DTG was unsurpassed in any head-to head clinical trials and not necessarily that it had superior efficacy or had surpassed its comparators.**

**The Panel noted that the interactive screens on the stand panel predominantly referred to DTG-based 2-drug regimens which were evaluated in non-inferiority studies (SWORD-1, SWORD-2, GEMINI-1 and GEMINI-2). In the Panel's view, non-inferiority studies evaluated whether one treatment was non-inferior to another treatment by a pre-specified margin. In this regard, the Panel queried the use of 'unbeaten' in the claim given that the material predominantly referred to DTG-based 2-drug regimens which were only supported by non-inferiority studies. This was reinforced by the layout and reading left to right would mean viewing the non-inferiority data first. Context was important. The Panel considered that the claim on the stand panel in question which was immediately followed by 'Tap to explore the dolutegravir (DTG) data' encompassed all DTG clinical trials, including DTG-based 3-drug regimens which had been evaluated in both superiority and non-inferiority studies. The Panel therefore considered the body of evidence for the claim ie both 2-drug and 3-drug DTG based regimens noting that there were a number of studies.**

**The Panel noted that Gilead had provided no evidence to suggest that there were ARV combinations that had surpassed either a 2-drug or a 3-drug DTG-based regimen in any head-to-head clinical trial.**

**The Panel noted that the screen in question contained no details of the patient populations in the studies and a user would have to click on the screen to access such information. In the Panel's view, this was not necessarily unacceptable provided that the information on the screen in question was not misleading. The Panel noted that both the Tivicay and the Juluca SPCs stated that these medicines should be prescribed by physicians experienced in the management of HIV infection.**

**The Panel noted its comments above and considered that although the claim 'Unbeaten in head to head**

**clinical trials' was a strong, broad claim, there appeared to be data to support it and the audience would not be misled. Gilead had not shown, on the balance of probabilities, that the claim on the stand panel in question was ambiguous, misleading or incapable of substantiation as alleged and the Panel therefore ruled no breach of the Code. The Panel did not consider that ViiV had failed to maintain high standards in this regard and ruled no breach of the Code.**

Gilead Sciences Europe Ltd complained about materials being used by ViiV Healthcare UK Ltd to promote Tivicay (dolutegravir) and Juluca (dolutegravir/rilpivirine). Tivicay was used in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV). Juluca was used in the treatment of HIV-1 infection in certain adults who were virologically-suppressed on a stable antiretroviral regimen for at least six months.

**1 Alleged off-label promotion of Tivicay**

**COMPLAINT**

Gilead stated that during the HIV Drug Therapy conference held in Glasgow, 28-31 October 2018, in the context of Tivicay promotion, ViiV promoted results from the GEMINI-1 and GEMINI-2 studies which investigated the efficacy and safety of dolutegravir (DTG) in combination with one other antiretroviral (ARV) agent, lamivudine (3TC), for the treatment of HIV in treatment naïve patients. Various claims accompanied the promotion of this combination (photographs of various exhibition panels were provided which included references to a two-drug regimen).

At the time of that promotion, Section 5.1 of the Tivicay summary of product characteristics (SPC) made reference to the following clinical studies, none of which investigated the use of DTG in combination with 3TC or any other combination of DTG with only one other ARV ('DTG based 2 drug regimens' or 'DTG based dual therapy') in treatment naïve patients:

- SINGLE (Walmsley et al (2013)) and SPRING-2 (Raffi et al (2013)) – studies of Tivicay once daily in combination with two nucleoside reverse transcriptase inhibitors (NRTIs), abacavir (ABC) and 3TC in HIV treatment naïve patients (ie 'DTG-based 3 drug regimens', alternatively named 'DTG-based triple therapy')
- FLAMINGO (Clotet et al (2014)) – study of Tivicay once daily in combination with two NRTIs (either ABC/3TC or emtricitabine/tenofovir disoproxil fumarate [FTC/TDF]) in HIV treatment naïve patients (ie a DTG-based 3 drug regimen, alternatively named DTG-based triple therapy)
- SAILING (Cahn et al (2013)– study of Tivicay once daily in combination with investigator selected background regimen consisting of up to 2 agents (including at least one fully active agent) in patients with prior treatment failure, but not exposed to the integrase class. The majority of patients were also taking a protease inhibitor [PI] in combination with Tivicay in this study.
- VIKING-3 (Castagna et al (2014)) – study of Tivicay 50mg twice daily in HIV-1 infected, ART-experienced adults with virological failure and current or historical evidence of raltegravir and/ or elvitegravir resistance (each being members of the integrase inhibitor class of ARVs). Patients received Tivicay 50 mg twice daily with the current failing background regimen for 7 days followed by optimised background ART from Day 8.

Gilead stated that on the first day of the conference (28 October), it contacted ViiV and asserted that the use of DTG in combination with only 3TC in the treatment of HIV was clearly off label, not in accordance with the terms of the Tivicay marketing authorization, and therefore in breach of Clause 3.2 of the Code. Gilead requested that any relevant material be removed immediately. ViiV's defence on site was that Tivicay could be promoted in combination with 3TC due to the so called 'broad' indication for Tivicay, namely 'Tivicay is indicated in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV) infected adults, adolescents and children above 6 years of age'. As a result, ViiV did not agree to remove reference to any claims pertaining to the combination of Tivicay with 3TC, and so these were consequently available for the duration of the conference. Gilead further alleged a breach of Clauses 2 and 9.1 of the Code.

Gilead stated that ViiV's major defence was centered on Tivicay having a so called 'broad' indication, asserting that dolutegravir could be used under any circumstances, as long as with at least one other antiretroviral agent. This position was clearly not supportable for the following reasons:

(i) The SPC contained essential information for the use of a medicine, agreed after a process of evaluation and based on the clinical trials presented as part of the marketing authorization application.

The structure and content of the SPC were harmonised in the European Union and the basic principles for the presentation of the information in the SPC were set out in the 'Guideline on Summary of Product Characteristics' of the European Commission.

For the therapeutic indication (Section 4.1), the European regulators had resolved that the indication should be stated clearly and concisely and should define the target disease or condition, the age group, distinguishing between treatment (curative/ symptomatic), prevention and diagnostic indication. In order to maintain the indications as concise as possible, it was resolved at the regulatory level in Europe that the data of the studies, must be included in Section 5.1, not in Section 4.1, of the SPC.

In this manner, the relevant clinical information supporting the authorised indication, in particular, the results of the clinical trials assessed by the regulatory bodies which support the authorised

indication(s), should be concisely presented in Section 5.1 of the SPC. The aim of Section 5.1 was to present information that was relevant to prescribers and healthcare professionals about the authorised indication to ensure that the medicine was used in an efficient and safe manner in clinical practice.

The interpretation of the conditions of authorised use should, therefore, not be based on the information contained in a single section of the SPC in isolation, but require the review of the SPC as a whole, as the relevant scientific information was found in different sections.

(ii) At the time Tivicay was granted a marketing authorization by the European Medicines Agency (EMA) with the aforementioned indication, no data existed on the use of dolutegravir in combination with one other antiretroviral agent in HIV treatment naïve patients. In fact, at that time, there were no antiretroviral regimens comprising of a total of 2 agents that were approved for the initial treatment of HIV.

(iii) The EMA Guideline on the clinical development of medicinal products for the treatment of HIV infection clearly outlined that the existing wording for the Tivicay indication was derived from the marketing authorisation holder having undertaken a study in patients with viral resistance relevant to the drug class of the agent being authorised. In other words, ViiV was able to obtain the aforementioned indication for Tivicay on the basis of the results of the VIKING-3 study, which investigated a completely different paradigm to the use of dolutegravir in combination with one other ARV in HIV treatment naïve patients. Specifically, VIKING-3 involved a double (bid) dose of Tivicay, and investigated this in combination with multiple other ARVs, in patients with a history of virological failure and resistance to the 'first generation' integrase inhibitors raltegravir and elvitegravir. Therefore, ViiV's argument that it was in accordance with the marketing authorization, and consistent with the Tivicay SPC, to promote new and unique combinations of DTG with just one other antiretroviral agent, that at the time of granting of the initial indication had not been assessed by EMA's Committee for Medicinal Products for Human Use (CHMP), was simply not correct.

Gilead stated that during the course of its follow up complaint, the Tivicay label was updated on 16 November to incorporate reference to the GEMINI studies. ViiV subsequently argued that as Sections 4.1 and 4.2 of the Tivicay SPC were not modified, this supported that the promotion of Tivicay in combination with 3TC during the Glasgow conference was appropriate. However, Gilead maintained that considering the nature of wording of the pre-existing indication available in the Tivicay SPC, clearly granted to ViiV on the basis of the results from the VIKING-3 study, the lack of change in Section 4.1 or 4.2 in itself did not validate ViiV's pre-license promotion of Tivicay with 3TC as a complete regimen for the treatment of HIV infection. In further support of the inappropriate interpretation of this indication by ViiV, Gilead noted that a new warning appeared in Section 4.4 of the Tivicay SPC following the Tivicay label update to incorporate the GEMINI data:

> **Lamivudine and dolutegravir**
> The two-drug regimen of dolutegravir 50 mg once daily and lamivudine 300 mg once daily was explored in two large randomized and blinded studies, GEMINI 1 and GEMINI 2 (see section 5.1). This regimen is only suitable for the treatment of HIV-1 infection where there is no known or suspected resistance to the integrase inhibitor class, or to lamivudine.

Gilead stated that this emphatically supported that the combination of Tivicay with lamivudine (3TC) as a complete regimen was not considered to be within the previous scope of the marketing authorisation at the time of the Glasgow HIV conference and that the promotion of the use of Tivicay in combination with only 3TC as a complete regimen was not consistent with the Tivicay SPC at the time. The inclusion of the warning in Section 4.4 of the SPC confirmed that in the opinion of the CHMP there was important safety information which prescribers needed to be aware of when contemplating treatment with a regimen of Tivicay with 3TC. The promotion of this combination before the CHMP had finalized its consideration of the label update and before knowledge of, and without, the important safety information that in the opinion of the CHMP needed to be provided to prescribers created the exact harm that Clause 3.2 was aimed at preventing.

Gilead stated that whilst ViiV acknowledged that Section 4.4 of the Tivicay SPC was updated following the Type 2 variation to include the GEMINI data, it argued that the promotional material in question included the study eligibility criterion which was subsequently added to Section 4.4, and therefore the target audience would have been fully aware of the study population of which the results were predicated. However, Gilead did not accept this defence. According to the EMA, the objective of Section 4.4 of the SPC was to provide information on a specific risk when health professionals had to be warned of this risk or the risk led to a precaution for use to avoid harm. Associated warnings should be clear, compelling and effective. Clearly, simply sharing the inclusion criteria of a study from a single Phase 3 program did not replace the absence of this warning being available in the Tivicay SPC during its promotion with 3TC during the Glasgow HIV Conference. The warning was absent at this stage, of course, as the promotion took place before the CHMP had approved the update to the Tivicay marketing authorization to include the GEMINI data and agreed the associated warning now included in the updated SPC. It was a fundamental principle of the Code that the prescribing information was provided in a clear and legible manner in all promotional material (Clause 4.1), including reference to any warnings issued by the licensing authority (Clause 4.2) so that prescribers had all the relevant information needed about the products promoted to them to inform their prescribing

decisions, and within the correct context.
In summary, Gilead alleged that the promotion of the combination of Tivicay with 3TC as a complete regimen by ViiV during the conference was not in accordance with the marketing authorization for Tivicay at the time, was inconsistent with the SPC for Tivicay at the time and was therefore in breach of Clause 3.2 of the Code. Given the serious nature of the matter Gilead further alleged breaches of Clauses 2 and 9.1.

**RESPONSE**

ViiV submitted that its commercial stand did promote the use of Tivicay in combination with lamivudine at the HIV Drug Therapy 2018 Conference in October 2018 based on the results of the GEMINI studies. However, contrary to the assertion of Gilead, this promotion was not inconsistent with the marketing authorisation at the time. ViiV denied breaches of Clauses 3.2, 9.1 and 2.

ViiV submitted that the indication for Tivicay did not mandate a minimum number of ARVs to be included in combination therapies.

In October 2018 at the time of the promotion, Section 4.1 (Therapeutic Indications) of the SPC for Tivicay read:

> 'Tivicay is indicated in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV) infected adults, adolescents and children above 6 years of age.'

ViiV submitted that this broad indication was based on a wide-ranging clinical study programme incorporating treatment naïve patients, those with resistance and those with very limited options. The indication aligned to the EMA guidance for the development of medicinal products for HIV infection. The EPAR (European Public Assessment Report) stated:

> 'Dolutegravir has demonstrated its efficacy in large scale studies covering previously untreated patients as well as those with advanced treatment histories and multi class resistance. In particular, a high barrier to resistance was demonstrated in the absence of integrase inhibitor class resistance.'

ViiV submitted that the indication wording was agreed with the EMA based upon these results and in line with the EMA's guideline on the content of the SPC, the indication for Tivicay listed the target disease as HIV, that it was for treatment (rather than eg cure) and included the age range. Other than the age range, the SPC did not restrict the patient population but it did include a restriction on how Tivicay should be used *('in combination with other anti-retroviral medicinal products')*. It did not specify which antiretroviral medicinal products or how many of them Tivicay must be combined with. This ensured that dolutegravir was not given as monotherapy rather than to ensure it was given with a specific number or types of other medicines.

Section 4.2 of the Tivicay SPC restricted prescription to clinicians experienced in the management of HIV. The indication therefore allowed experts the flexibility to use Tivicay at all stages of the disease and to adjust regimens to suit clinical need in individual cases where there may be tolerability or resistance issues.

In 2018 ViiV applied to update the marketing authorisation for Tivicay with the data from the GEMINI studies. This resulted in changes to the SPC and in particular to Section 5.1 (Pharmacodynamic Properties) and Section 4.4 (Special Warnings and Precautions for Use). There was no change to Section 4.1 (Therapeutic Indications) or Section 4.2 (Posology). The changes to the SPC came into effect on 15 November 2018.

ViiV submitted that regulations required only that promotion was not inconsistent with the marketing authorisation, not that promotion could only rely on data within the SPC.

Within its complaint, Gilead described in some detail the studies listed in Section 5.1 of the Tivicay SPC at the time of the conference in question. All of the studies listed featured use of Tivicay in combination with two or more ARVs and ViiV readily acknowledged that fact.

ViiV submitted that where it differed with Gilead was in Gilead's belief that the therapeutic indication of a medicine can only be promoted in the strict context of the studies that were mentioned in Section 5.1.

Clause 3.2 of the Code stated that promotion 'must not be inconsistent with the particulars listed in the summary of product characteristics.' It did not state that the studies being used to support promotion must be in the SPC. This was in line with the Medicines and Healthcare products Regulatory Agency (MHRA) position as stated in the Blue Guide:

> 'An advertisement may include statements not included in the SPC provided these can be substantiated and are not inconsistent with the SPC information'.

ViiV submitted that in the GEMINI studies, the regimen of Tivicay and lamivudine was used for the treatment of HIV in adults. This fitted squarely within the elements of the indication, namely, the treatment of HIV as part of combination therapy in adults. Accordingly, ViiV submitted that use of Tivicay with lamivudine as a complete regimen for the treatment of HIV did not violate Clause 3.2 of the Code. Moreover, there was nothing in the Tivicay SPC at the time that precluded its use with one other antiretroviral. The indication allowed for combined treatment and there were no contraindications or special warnings and precautions regarding the use of Tivicay in two drug regimens. ViiV maintained that the claims it made in October 2018, related to the GEMINI data, were not inconsistent with the relevant particulars of the SPC at the time.

ViiV submitted that following the update to the SPC for Tivicay in November 2018 Sections 4.1 (Therapeutic Indications) and 4.2 (Posology) remained unchanged. As the GEMINI data provided new information for health professionals it was

submitted for inclusion within the Tivicay label. When the Tivicay SPC was updated with the GEMINI data, no changes were made to the therapeutic indication or posology for Tivicay in Sections 4.1 and 4.2 of the SPC.

The SPC Guidelines from the EMA, and referred to by Gilead, made it clear that updates to Section 5.1 (Pharmacodynamic properties) of the SPC could only take place if they were consistent with the indication as described in Section 4.1 as follows:

> 'Where results from subsequent studies provide further definition or information on an authorised indication, such information, provided it does not itself constitute a new indication, may be considered for inclusion in section 5.1.'

ViiV submitted that the fact that Section 5.1 was updated to include the results of the GEMINI studies supported ViiV's position that the use of Tivicay and lamivudine was consistent with the marketing authorisation. Finally, the fact that Section 4.4 of the SPC was updated in connection with the Type 2 variation did not retroactively make ViiV's use of the GEMINI data inappropriate. The need to exercise care in treating people living with HIV with resistance was well-known to physicians and the inclusion criteria for the GEMINI studies were communicated clearly within the stand materials.

ViiV submitted that it was responsible and appropriate that companies were allowed to inform health professionals of important updates to the safety or efficacy of a medicine within its licensed indication prior to an update to the SPC.

The SPC was a living document. It was updated throughout the life of a product to ensure it provided relevant current information to health professionals. However, there would be an inevitable time lag between new data being available and it being incorporated in to the SPC. During that period, sharing important information with prescribers was reasonable as long as the data being incorporated was not inconsistent with the information in the SPC. Common examples would be new drug interactions or additional side effects that might come to light during use of the medicine within its licensed indication. ViiV therefore refuted all allegations of breaches of Clause 3.2, 9.1 and 2.

ViiV noted Gilead's submission that the update to Section 4.4 (Special warnings and precautions for use) of the Tivicay SPC which resulted from the variation supported a view that promotion of the combination in October was outside the terms of the marketing authorisation. ViiV disagreed; its view was that it had significant new information about in-licence use of Tivicay available from the GEMINI studies and it was reasonable to communicate this to expert HIV physicians attending the international congress given that it was not inconsistent with information in the SPC at the time but only added to it. The wording that entered Section 4.4 of the SPC for Tivicay in November 2018 based on the GEMINI studies was as follows:

> **'Lamivudine and dolutegravir**
> The two-drug regimen of dolutegravir 50 mg once daily and lamivudine 300 mg once daily was explored in two large randomized and blinded studies, GEMINI 1 and GEMINI 2 (see section 5.1). This regimen is only suitable for the treatment of HIV-1 infection where there is no known or suspected resistance to the integrase inhibitor class, or to lamivudine.'

ViiV submitted that at the time of the October conference the final wording, that would enter the SPC as a result of the variation, was not approved. As acknowledged by Gilead the information that the study populations consisted only of those with, 'no major RAMS [resistance associated mutations]' was included clearly in the congress stand materials, and as such promoted the rational use of medicines and did not put patients at risk. The actual language on the stand could be considered to be more restrictive than the update to the wording in Section 4.4 of the SPC as it covered all major resistance mutations to any class of HIV medicine. The eventual wording in Section 4.4 restricted only with known or suspected resistance to integrase inhibitors and lamivudine. Other entry criteria such as a baseline screening RNA of <500,000 copies per ml were also stated on materials.

ViiV noted that as pointed out by Gilead, prescribing information must also include 'any warning issued by the Medicines Commission, the Commission on Human Medicines, the Committee on Safety of Medicines or the licensing authority' but they did not include the rest of the sentence which stated 'which is required to be included in advertisements'. There were no specific warnings in the Tivicay SPC that the licensing authority had required to be included in advertisements either at the time of the conference or currently.

ViiV submitted that it was unsure as to whether Gilead was alleging breaches of Clauses 4.1 and 4.2. For clarity, the prescribing information for Tivicay that was current at the time of the congress was freely available during promotional activities. Clearly it could not, at that time, contain the new safety or efficacy information related to combination use with lamivudine as the SPC was yet to be updated. ViiV therefore denied a breach of Clause 4.1 or 4.2 if alleged.

**PANEL RULING**

The Panel noted Gilead's allegation that ViiV had promoted Tivicay (dolutegravir (DTG)) outside the terms of its marketing authorization at a conference in October 2018 by promoting the GEMINI-1 and GEMINI-2 studies which evaluated DTG in combination with just one other anti-retroviral agent, lamivudine (3TC), together with various accompanying claims. Gilead did not refer to specific materials but provided photographs of exhibition stand panels which it stated were 'some examples'. The Panel therefore considered the allegation in general and not in the context of any specific materials at the conference in question. The Panel noted that Clause 3.2 of the Code stated that the promotion of a medicine must be in accordance with the terms of its marketing authorization and must not be inconsistent with

the particulars listed in its summary of product characteristics (SPC).

The Panel noted that the indication in Section 4.1 of the Tivicay SPC stated:

> 'Tivicay is indicated in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV) infected adults, adolescents and children above 6 years of age'.

The Panel noted that the indication in Section 4.1 did not specify a minimum or a maximum number of ARV medicines that Tivicay should be combined with. Section 4.2 (posology and method of administration) stated that Tivicay should be prescribed by physicians experienced in the management of HIV infection. Section 5.1 (pharmacodynamic properties) referred to various combinations of DTG with other ARV medicines including 3TC.

The Panel noted Gilead's assertation that at the time Tivicay was granted a marketing authorization for the above indication, no data existed on the use of DTG in combination with one other ARV agent in HIV treatment naïve patients. ViiV acknowledged that all the studies listed in Section 5.1 of the Tivicay SPC at the time of the conference featured use of DTG in combination with two or more ARV agents.

The Panel noted that at the time of the conference, the Tivicay SPC did not refer to the GEMINI studies. According to ViiV, following the conference, in November 2018, the SPC was updated to include, *inter alia*, GEMINI-1 and GEMINI-2 study results in Section 5.1 and information based on these studies was included in Section 4.4 (special warnings and precautions for use) which stated:

> **'Lamivudine and dolutegravir**
> The two-drug regimen of dolutegravir 50 mg once daily and lamivudine 300 mg once daily was explored in two large randomized and blinded studies, GEMINI 1 and GEMINI 2 (see section 5.1). This regimen is only suitable for the treatment of HIV-1 infection where there is no known or suspected resistance to the integrase inhibitor class, or to lamivudine'.

The Panel noted Gilead's assertation that the update to Section 4.4 of the Tivicay SPC supported the company's view that the combination of Tivicay with lamivudine as a complete regimen was not considered to be within the scope of the marketing authorization at the time of the conference and that this SPC update constituted important safety information which prescribers needed to be aware of when considering a regimen of Tivicay plus lamivudine.

The Panel noted ViiV's submission that the information regarding the GEMINI studies on the exhibition stand at the conference could be considered more restrictive than the subsequent SPC update to Section 4.4 as it covered the exclusion of patients with all major resistance mutations to any class of HIV medicine and referred to other study entry criteria such as a baseline screening RNA of <500,000 copies per ml.

The Panel further noted ViiV's submission that when the SPC was updated with the GEMINI studies, no changes were made to Section 4.1 (therapeutic indications) or Section 4.2 of the SPC.

In the Panel's view it was not necessarily unacceptable to promote a medicine using studies that were not listed in its SPC as long as such data was not inconsistent with the particulars listed in the SPC. In the Panel's view, using Tivicay in combination with one other ARV medicine in HIV was not in itself inconsistent with the indication for Tivicay to be used in combination. Physicians might decide not to use a two drug-regimen prior to the availability of data.

The Panel noted its comments above and considered that Gilead had not proved, on the balance of probabilities, that ViiV's promotion of Tivicay in combination with lamivudine at the October 2018 conference in general, constituted promotion of Tivicay outside the terms of its marketing authorization or in a manner that was inconsistent with its SPC. No breach of Clause 3.2 of the Code was ruled. The Panel noted that any allegations in relation to specific materials would be considered on their own particular merits.

The Panel did not consider that ViiV had failed to maintain high standards and ruled no breach of Clause 9.1.

Clause 2 was a sign of particular censure and was reserved for such use. The Panel noted its rulings of no breach above and consequently ruled no breach of Clause 2.

**2 Alleged use of Tivicay data in combination with two antiretroviral agents to support promotion of Tivicay with one antiretroviral agent**

**COMPLAINT**

(i) General use of data on dolutegravir (DTG) combined with two antiretroviral agents to support promotion of DTG with one antiretroviral agent, including the claim 'Only dolutegravir has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens' [ UK/DTGRPV/0033/18(3)]

Gilead stated, as background, since 1996, in patients without virological resistance, the foundation of HIV management had been built upon the use of 3 antiretroviral agents, comprising of 2 NRTIs and a third agent (together known as Highly Active Antiretroviral Therapy [HAART], or triple therapy). To this day, all major international HIV guidelines still preferentially recommended regimens with 3 active antiretroviral agents based on 2 NRTIs and a third agent for the initial treatment of HIV.

Gilead stated that the integrase inhibitor, dolutegravir, had been investigated as the third agent using this triple therapy paradigm in several treatment naïve studies (SINGLE, SPRING-2,

FLAMINGO), which contributed to the initial (or early) Tivicay marketing authorization. In two of these studies (SINGLE, FLAMINGO), dolutegravir combined with 2 NRTIs (ie DTG-based triple therapy) demonstrated statistically superior efficacy versus comparator (when also combined with 2 NRTIs) in an intent-to-treat analysis at the 48 week primary endpoint. In addition, in the SAILING study, dolutegravir taken once daily in combination with an investigator selected background regimen consisting of up to 2 agents (including at least one fully active agent) in patients with prior treatment failure, but not exposed to the integrase class, dolutegravir was found to have statistically superior efficacy in an intent-to-treat analysis versus comparator at the primary endpoint. In the SAILING study, 71% of patients had at least 2 active agents as background in addition to dolutegravir, and at least 64% of patients were also administered a ritonavir-boosted protease inhibitor (PI/r).

Gilead stated that as a consequence of the results of the SINGLE, SPRING-2 and FLAMINGO studies, dolutegravir was preferentially recommended in all major international HIV guidelines in combination with various NRTI backbones (ie in a combination with 2 NRTIs to form a DTG-based triple therapy) for the initial treatment of HIV.

Gilead stated that more recently, dolutegravir had been studied in combination with rilpivirine in the SWORD study (ie studied as a DTG based 2-drug regimen or DTG-based dual therapy). In the SWORD study, HIV-1 infected adults who were virologically-suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen for at least six months with no history of virological failure and no known or suspected resistance to any non-nucleoside reverse transcriptase inhibitor (NNRTI) or integrase inhibitor were randomized to remain on their baseline regimen or switch to a combination of dolutegravir and rilpivirine. The limited nature of this population was reflected in the Juluca (dolutegravir/rilpivirine) SPC indication. In this study, the switch to dolutegravir/rilpivirine demonstrated non-inferior efficacy versus remaining on background regimen over 48 weeks in these participants with HIV suppression at baseline.

In addition, dolutegravir had recently been studied in combination with 3TC in participants (≥18 years) with HIV-1 infection and a screening HIV-1 RNA of 500,000 copies per mL or less, and who were naive to antiretroviral therapy (the GEMINI study). At week 48, in the pooled GEMINI intention-to -treat-exposed population, non-inferior efficacy was demonstrated with dolutegravir and 3TC compared with once-daily dolutegravir plus 2 NRTIs.

Gilead stated that a review of the above studies demonstrated that the SWORD and GEMINI studies differed substantially from the SINGLE, SPRING-2, FLAMINGO and SAILING studies on multiple important aspects:

- SINGLE, SPRING-2, FLAMINGO involved the use of dolutegravir in combination with 2 other antiretroviral agents (2 NRTIs), whereas SWORD and GEMINI each involved the use of dolutegravir in combination with 1 other antiretroviral agent. In SWORD, dolutegravir was combined with rilpivirine, an NNRTI, whereas in GEMINI, dolutegravir was combined with 3TC, an NRTI. In both the SWORD and GEMINI studies, the combinations of DTG plus rilpivirine and DTG plus 3TC were respectively considered investigational regimens, tested against standard of care triple therapy.
- The SINGLE, SPRING-2, FLAMINGO studies did not specify an upper limit on baseline HIV-1 RNA viral load at study entry. In contrast, the GEMINI study required that treatment naïve patients had a baseline screening HIV-1 RNA of 500,000 copies per mL or less. In the field of HIV, there were multiple examples where certain ART combinations had performed less favourably in patients with higher baseline viral load, and in many cases this feature has heavily influenced how guidelines committees viewed the utility of various HIV regimens, as reflected by their positioning within HIV treatment guidelines.
- The SWORD study was restricted to HIV-1 infected adults who at baseline were virologically-suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen for at least six months with no history of virological failure and no known or suspected resistance to any non-nucleoside reverse transcriptase inhibitor or integrase inhibitor. As already mentioned, the specificity of this population was reflected in the indication of the dolutegravir/rilpivirine (Juluca) SPC.
- The SAILING study involved the use of dolutegravir taken once daily in combination with an investigator selected background regimen consisting of up to 2 agents (including at least one fully active agent) in patients with prior treatment failure, but not exposed to the integrase class. 71% of patients had at least 2 active agents as background in addition to dolutegravir, and at least 64% of patients were also administered a ritonavir-boosted protease inhibitor (PI/r). This was clearly a different population to those who were studied in GEMINI or SWORD, considering patient baseline characteristics, clinical history, and the number and nature of ARVs used across these studies.

Gilead stated that despite the important differences described in the various studies above, in the context of promotion of Juluca and Tivicay plus 3TC, ViiV had developed material which made claims about data on DTG with two antiretroviral agents (DTG-based triple therapy) to support promotion of DTG with one antiretroviral agent (DTG-based dual therapy). Gilead alleged that use of data in this fashion breached Clauses 7.2, 7.3, 7.4 and 9.1 of the Code.

**Item UK/DTGRPV/0033/18(3)-'Only dolutegravir has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens'**

Gilead stated that the above claim appeared in the context of the promotion of Tivicay + 3TC (item UK/DTGRPV/0033/18(3) available on the UK ViiV Exchange website (https://uk.viivexchange.com/our-medicines/2dr/). Gilead alleged that this claim when used in the context of the promotion of two drug regimens was in breach of Clauses 7.2 and 7.4 of the Code.

The claim 'Only dolutegravir has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens' was used to support the overarching question 'What makes DTG an ideal core agent to power a 2DR?'. This gave the clear misleading impression that results with DTG based 3 drug regimens might also be applied when DTG was given as part of a 2 drug regimen, especially when considering the relative prominence of '2DR' in the title, compared with '3-drug regimen' in the smaller copy, and the clear promotional focus of item UK/DTGRPV/0033/18(3) toward DTG-based 2 drug regimens. Furthermore, throughout the course of intercompany dialogue, ViiV had not been able to substantiate that the results observed in either the GEMINI or SWORD studies were because of any efficacy data that were generated with DTG when given as part of a 3 drug regimen, and as such ViiV had not been able to substantiate the impression given by the use of this claim in the two drug regimen context.

Gilead stated that during inter-company dialogue, ViiV had stated that the claim 'Only dolutegravir has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens' made it immediately clear to readers that it related to 3 drug regimens only and was therefore unambiguous, and also stated that previous 2 drug regimens had shown variable efficacy, and therefore it was important to contextualise why a DTG based 2 drug regimen was different to previous 2 drug regimens. For the reasons indicated above, Gilead did not accept that including the words 'as part of a 3 drug regimen' removed the misleading impression that the superior efficacy would also be seen with the two drug regimens being promoted. In addition, to state that 'it is important to contextualise why a DTG based 2 drug regimen is different from previous 2 drug regimens' was in itself incapable of substantiation as there was no available data directly comparing DTG based 2 drug regimens with 2 drug regimens that did not contain DTG. While ViiV correctly stated that previous 2 drug regimens had shown variable efficacy, there was no direct evidence in the literature to support that 2 drug regimens that had demonstrated lower efficacy in clinical trials were expected to do so based on their performance as part of 3 drug regimens. In summary, Gilead asserted that the only claim that should be made regarding promoted regimens or combinations - in this case Tivicay and 3TC, or Juluca should be restricted to the evidence that had been generated with those specific regimens. Gilead alleged that failure to do so was a breach of Clauses 7.2, 7.3 and 7.4 of the Code. Gilead did not consider that high standards had been maintained and alleged a breach of Clause 9.1.

*(ii) 'Unbeaten in head to head clinical trials'*

Gilead stated that the claim 'Unbeaten in head to head clinical trials' was also made at the ViiV stand during the Glasgow HIV Conference. Despite Gilead's request to have this claim removed during a face to face discussion with ViiV on 29 October, it remained on display during the entire course of the conference.
Gilead stated that during the course of inter-company dialogue, it highlighted multiple issues associated with this claim, namely:

- That health professionals were required to click through on the main display in order to understand the basis of the claim was alleged to be in breach of Clause 7.2 in that the claim was ambiguous and not capable of standing alone. This main display was clearly visible to all conference delegates in a high traffic area, with only a nominal percentage likely pausing to click through to review the material in its entirety. Through the course of intercompany dialogue, ViiV stated that there was no requirement for the reader to 'click through' to understand the statement 'unbeaten in head to head clinical trials', however this did not appear to be the case. The page in question was prominent and required the reader to 'tap' to explore the dolutegravir (DTG) data. Thus, without audience interactivity, this page was essentially all the audience would read, and therefore any relevant claims must clearly and prominently be capable of being substantiated from the information within this page. This was not the case.
- The evidence used to support this claim (not visible on the main initial panel) was from 10 clinical trials of DTG in various combinations and populations and 4 clinical trials when used as a two-drug regimen. A review of all the content at the ViiV stand showed a clear promotional focus on DTG in combination with either rilpivirine or 3TC. Consequently, similar to Point 2 (i) above, Gilead alleged that the use of data derived from DTG-based triple therapy studies to support this claim in the context of DTG-based dual therapy promotion was ambiguous, misleading and gave the impression that the attributes of dolutegravir seen in the triple therapy studies were also delivered when dolutegravir was used as part of a two drug regimen. Gilead alleged that this was in breach of Clauses 7.2, 7.4, and 9.1 of the Code
- The claim 'unbeaten' was in itself misleading, ambiguous, and did not compare medicines for the same needs or intended for the same purpose and was therefore alleged to be in breach of Clauses 7.2, 7.3, 7.4 and 9.1 of the Code. ViiV stated that 'unbeaten' was defined by the Oxford Dictionary as meaning 'not surpassed or undefeated'. However, this definition clearly did not exclude the potential that the promoted regimens might have actually surpassed or defeated the comparator in some instances, thus highlighting the ambiguity of the claim. While this ambiguity was exacerbated by the fact that ViiV had used data on DTG-based triple therapy to support the claim (which had surpassed comparator in the measure of efficacy in some instances), the fact that DTG-based 2 drug regimens had never surpassed comparator in any clinical studies (Gilead speculated for the measure of efficacy), also rendered the claim misleading. Even if taking a more conservative approach, where a reader might interpret the claim as meaning 'has not been beaten' and restricted to studies that included DTG-based 2 drug regimens, the claim was still an overstatement as the piece in question did not adequately specify the restricted populations in which Juluca or Tivicay + 3TC were studied, in the SWORD and GEMINI studies respectively.

Instead, it gave the misleading impression that the promoted combinations were unbeaten across all populations in which triple therapies had been studied. While Gilead did not expect that a specific regimen was required to be studied against every possible combination or permutation of HIV medicines in order to be able to potentially make these types of all-encompassing claims, in this particular case there were some clear exclusion criteria for each of the SWORD and GEMINI studies that must be clearly made prominent if considering making any claims versus standard of care regimens; specifically, in SWORD (Juluca), patients were required to be virologically-suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen for at least six months with no history of virological failure and no known or suspected resistance to any non-nucleoside reverse transcriptase inhibitor or integrase inhibitor, whereas in GEMINI (Tivicay plus 3TC), patients were excluded if their baseline HIV-1 RNA exceeded 500,000 copies/ml, and patients with genotypic resistance to any class of drugs were excluded (as opposed to just within the drug classes being studied). These types of restrictions did not apply to standard of care triple therapy.

- In addition, as already raised in Point 1, Gilead alleged that any proactive discussion of the use of Tivicay + 3TC during the Glasgow conference was in breach of Clause 3.2 of the Code and Gilead did not accept that any references citing this combination should have been used to support this or any claim during the Glasgow conference.

**RESPONSE**

ViiV did not accept that it was in breach of the Code in respect of any of the allegations made by Gilead.

(i) General use of data on dolutegravir combined with two antiretroviral agents to support promotion of dolutegravir with one antiretroviral agent

ViiV stated that Gilead had gone to some lengths in its complaint to point out the differences between the various studies involving dolutegravir in combination with other ARVs. In particular, they had highlighted the differences between the studies involving dolutegravir in a three-drug regimen and those where it was a part of a two-drug regimen and alleged 'that use of data in this fashion breaches Clauses 7.2, 7.3, 7.4 and 9.1'. However, Gilead did not make clear exactly in what way each of those clauses were breached. As ViiV understood it, the complainant had the burden of proof with respect to how the use of the data was misleading (Clause 7.2), in what way a comparison was inappropriate (Clause 7.3), how the information was not capable of substantiation (Clause 7.4) and in what way high standards had not been maintained (Clause 9.1).

Tivicay was indicated in combination with other antiretrovirals as a treatment for HIV and ViiV promoted its use in both three and two drug regimens as new data continued to be produced. ViiV submitted that treatments for HIV infection, although highly effective in suppressing viral replication, had the potential for significant side effects. Thus, whilst therapy with three ARVs had been the mainstay of treatment for most patients, clinicians and researchers had naturally questioned whether two-drug regimens could work equally well. Unfortunately, when two-drug regimens were first studied, although better than monotherapy, they had limited efficacy because only one class of drug (NRTI) was available at the time. This meant that the HIV virus was attacked at only one point in its lifecycle and resistance to treatment could develop more readily. It was not until the introduction of new classes of ARVs, which when used in combination could target the virus in two different ways, that HIV therapy became substantially more effective. This two-pronged approach to the virus lifecycle had been the mainstay of HIV treatment and was recommended in all major treatment guidelines. For most people this involved taking a three-drug ARV regimen.

ViiV submitted that since its introduction, dolutegravir had become integral to guideline recommended three-drug ARV regimens for a wide range of patients. In combination it had shown superiority over comparators in a number of three-drug regimens, and resistance had only rarely been observed both in clinical trials and real-world settings. In every phase 3, head to head study that dolutegravir had been included in, the results had either shown dolutegravir based regimens to be superior or non-inferior in comparison with regimens based on other ARVs. No combination of ARVs had shown superiority over a dolutegravir based regimen in any head-to-head clinical trial in any patient population. It was this history that the materials conveyed as context to the promotion of dolutegravir based two-drug regimens. It was to reassure the prescriber that two-drug regimens based on dolutegravir were not the same as historical two-drug regimens.

ViiV submitted that it was not suggesting, as Gilead implied, that the superior efficacy results observed in studies in some dolutegravir based three-drug regimens could be extrapolated directly to its use in two-drug regimens. ViiV was clear in all cases that the results from the GEMINI studies showed non-inferiority. Importantly the comparator arm in the GEMINI studies was also a dolutegravir-based three drug regimen (DTG+ tenofovir disoproxil fumarate and emtricitabine TDF/FTC). The inclusion of three drug regimen dolutegravir data provided context about the 'gold standard' nature of the comparator arm and thus provided reassurance. It was also clear to the readers (expert HIV physicians) which studies were using 3 drug regimens and which were using two drug regimens.

ViiV rejected the assertion by Gilead that providing context around dolutegravir based therapies was ambiguous or misleading in breach of Clause 7.2. ViiV also rejected the alleged breach of Clause 7.3 and was unsure in what way an unfair comparison was being made and with respect to what medicines.

ViiV submitted that its materials were clear that DTG+3TC and JULUCA were non-inferior. Its claims with respect to use of dolutegravir in two-drug or three-drug regimens were substantiated fully by the study data quoted and consequently it rejected a breach of Clause 7.4.

ViiV submitted that information regarding the use of dolutegravir in three-drug regimens was both fully substantiated and justified to provide context to the use of dolutegravir in two-drug regimens and that it had maintained high standards in communicating this. ViiV denied a breach of Clause 9.1.

**'Only dolutegravir has shown superior efficacy vs 5 different ART comparators when evaluated as part of a 3-drug regimen' – Item VIIV/DTGRPV/0033/18(3)**

ViiV noted Gilead's allegation that use of the statement above, in response to a question in the item asking why dolutegravir was chosen as the 'core agent' in a two-drug regimen in some way implied that the superior efficacy observed in three-drug regimen studies could be applied to the two-drug regimen of dolutegravir and lamivudine. ViiV rejected this interpretation. The reader was left in no doubt that the claim was related to use of dolutegravir as part of a three-drug regimen as it was clearly stated as such within the claim itself. It was impossible to see how a specialist in the management of HIV would, from that statement, assume that dolutegravir had shown superior efficacy versus comparators when used as part of a two-drug regimen. The claim was unambiguous and fully substantiated by the references used; ViiV denied breaches of Clauses 7.2 and 7.4. No comparisons were being made except between dolutegravir based regimens and the comparator regimens mentioned in the claim and those were all fully referenced and substantiated. ViiV therefore denied a breach of Clause 7.3. ViiV had maintained high standards in its communication about the use of dolutegravir as a basis for a two-drug regimen and therefore it denied a breach of Clause 9.1.

**(ii) 'Unbeaten in head-to-head clinical trials' – Claim used on the promotional booth at the HIV Drug Therapy 2018 Conference in Glasgow**

ViiV submitted that the claim at issue was the headline to a screen on an interactive panel with a subheading inviting physicians to tap to explore dolutegravir data. The stand itself was fundamentally promoting Tivicay. Tivicay was indicated in combination with other anti-retroviral medicinal products for the treatment of HIV infected adults, adolescents and children above 6 years of age. As such it could be used with a number of different ARVs in all types of HIV patients. It was not contrary to the Code for a company to promote different ways of using its product as long as it was not inconsistent with the SPC and compliant with the Code.

Contrary to Gilead's assertion, the claim was capable of standing alone even without tapping on the data. In every single head to head trial that dolutegravir had been in, either as part of a 3 drug regimen or a 2 drug regimen, the results showed that it had always matched or surpassed its comparators and Gilead did not dispute this. A 2015 review of the pharmacology, efficacy and safety of dolutegravir stated that it was '… equivalent or superior to existing treatment regimens in both treatment-naïve and treatment-experienced patients including those with previous raltegravir or elvitegravir failure'. Studies in the intervening years continued to support this.

Whether those reading the claim tapped on the screen to find out more information or not, they were not misled about the clinical trial outcomes data for dolutegravir based therapy. The Code required that all information, claims and comparisons must be capable of substantiation but there was no requirement that the substantiation must appear on the same page.

Clause 7.5 made clear that 'Substantiation for any information, claim or comparison must be provided as soon as possible, and certainly within ten working days, at the request of members of the health professions or other relevant decision makers'. The claim could stand alone, was unambiguous, and fully capable of substantiation. ViiV therefore denied a breach of Clause 7.2.

ViiV noted that Gilead alleged breaches of Clauses 7.2, 7.4 and 9.1 in that the claim 'gives the impression that the attributes of dolutegravir seen in triple therapy are also delivered when dolutegravir is used as part of a two-drug regimen'. The claim was true whether one was considering dolutegravir in a two-drug or three-drug based regimen. ViiV was not suggesting that the superior efficacy results observed in some dolutegravir based three drug regimen studies could be extrapolated directly to its use in two-drug regimens. The claim, in common with the other claims at issue, conveyed the strength of the data with respect to dolutegravir based therapy, when dolutegravir was used in a manner consistent with its broad marketing authorisation. ViiV consequently believed the claim to be accurate and capable of substantiation and denied breaches of Clauses 7.2, 7.4 and 9.1.

With regard to the use of the word 'unbeaten', ViiV rejected Gilead's allegations and submitted it did not imply superiority and did not imply the studies were taking place in the same populations of patients. The word 'unbeaten' was simply stating that dolutegravir based therapy had in no instance been shown to be inferior to any comparator regimen across all the patient groups it has been tested. All those patient groups fell within the licensed indication for dolutegravir.

The screen in question contained no details of the patient populations in the studies that led to the claim, but the claim was nevertheless true and those wishing to understand the substantiating evidence could explore the data in detail. The screen made no reference to superiority and contained three buttons which allowed clinicians the opportunity to view the GEMINI data, the SWORD data or the depth and breadth of DTG clinical trial data.

With regard to Gilead's view that the claim 'unbeaten' in the sense of 'has not been beaten'

was 'an overstatement as the piece in question did not adequately specify the restricted populations in which Juluca or Tivicay + 3TC were studied in the SWORD and GEMINI studies respectively' and stated that these 'types of restrictions do not apply in standard of care triple therapy', ViiV submitted in response that all randomised controlled clinical trials had populations restricted in some way and this fact was entirely understood by health professionals.

Within the HIV therapy area it was inconceivable that an expert physician viewing this claim would assume that all the studies referred to identical patient populations.

There was no precedent by which claims based on a clinical trial must be explicitly accompanied with all inclusion and exclusion criteria from that trial. They must be accurate of themselves, not mislead and be based on study populations consistent with the marketing authorisation. All this was true for the claim 'Unbeaten in head-to-head studies' with respect to both two- and three-drug dolutegravir regimens.

ViiV noted Gilead's implication that some special case should be made in the case of dolutegravir two-drug regimen claims as the 'types of restrictions' in the SWORD and GEMINI studies did not apply in three-drug regimens. This, however, was patently not the case. The licences for several antiretrovirals including Gilead medicines used as three-drug therapy demonstrated restrictions which came about as a result of the entry criteria for clinical studies, for instance:

- Odefsey was indicated for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35 kg) infected with human immunodeficiency virus-1 (HIV-1) without known mutations associated with resistance to the non-nucleoside reverse transcriptase inhibitor (NNRTI) class, tenofovir or emtricitabine and with a viral load ≤ 100,000 HIV-1 RNA copies/mL
- Atripla was indicated for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years and over with virologic suppression to HIV-1 RNA levels of < 50 copies/ml on their current combination antiretroviral therapy for more than three months. Patients must not have experienced virological failure on any prior antiretroviral therapy and must be known not to have harboured virus strains with mutations conferring significant resistance to any of the three components contained in Atripla prior to initiation of their first antiretroviral treatment regimen
- Biktarvy was indicated for the treatment of adults infected with human immunodeficiency virus-1 (HIV-1) without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

ViiV submitted that the claim 'unbeaten in head-to-head clinical trials' in respect of dolutegravir based therapy was consistent with the evidence for all two- and three-drug dolutegravir based therapies and it was not making a comparison. ViiV denied a breach of Clauses 7.2, 7.3, 7.4 and 9.1.

**PANEL RULING**

(i) General use of data on DTG combined with two antiretroviral agents to support promotion of DTG with one antiretroviral agent

The Panel noted that item VIIV/DTGRPV/0033/18(3) was a webpage on the ViiV exchange website with a focus on 2-drug regimens. The webpage included the subheading 'What makes DTG an ideal core agent to power a 2DR [2-drug regimen]?'. Below this, in smaller font, it stated 'Only dolutegravir…' followed by a number of claims including: 'Has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens'; and 'Is PROVEN EFFECTIVE in 2-drug regimens with lamivudine in treatment-naïve adult patients at 48 weeks and rilpivirine in virologically suppressed patients at 100 weeks'. 'SUPERIOR EFFICACY' and 'PROVEN EFFECTIVE' in the above two claims were in a different coloured font to the surrounding text.

The Panel noted that below this section of the webpage was a 'learn more' section which stated 'Explore dolutegravir-based, 2-drug regimens for your diverse patient needs' followed by the logos for Tivicay + lamivudine and Juluca.

The Panel noted Gilead's allegation that the claim in question 'Only dolutegravir…Has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens' in the context of the promotion of two-drug regimens gave the misleading impression that results with DTG-based three-drug regimens might also be applied when DTG was given as part of a 2-drug regimen considering the relative prominence of '2DR' in the title compared with '3-drug regimens' in the smaller font and the promotional focus of the webpage on 2-drug regimens.

The Panel noted ViiV's submission that the claim in question was not suggesting that the superior efficacy results observed in some DTG based 3-drug regimen studies could be extrapolated directly to its use in 2-drug regimens and that the claim was related to use of DTG as part of a three-drug regimen which was clearly stated and substantiated by the references.

The Panel noted that both the Tivicay and the Juluca SPCs stated that these medicines should be prescribed by physicians experienced in the management of HIV infection. The Panel considered the immediate and overall impression to an HIV physician. In the Panel's view, although the claim in question featured on a webpage promoting DTG-based 2-drug regimens, it appeared beneath the question of what made DTG an ideal core agent to power a 2-drug regimen. In the Panel's view it was clear that 'SUPERIOR EFFICACY' in the claim 'Only dolutegravir…Has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens' was in relation to DTG as a core agent in a 3-drug regimen and not in relation to a 2-drug regimen as alleged. An associated claim stated that DTG was '…PROVEN EFFECTIVE…' in two specific 2-drug regimens in certain patients. In this regard, the Panel considered that the intended

audience would not be misled as alleged. Gilead had not shown, on the balance of probabilities, that the claim 'Only dolutegravir…Has shown SUPERIOR EFFICACY vs 5 different ART comparators when evaluated as part of a 3-drug regimens' was misleading or incapable of substantiation and the Panel therefore ruled no breach of Clauses 7.2, 7.3 and 7.4.

The Panel did not consider that ViiV had failed to maintain high standards in this regard and ruled no breach of Clause 9.1.

(ii) 'Unbeaten in head to head clinical trials'

The Panel noted that the claim at issue appeared on an interactive stand panel at the ViiV stand at the HIV Drug Therapy 2018 conference, as referred to above at Point 1.

The stand panel was headed 'Unbeaten in head to head clinical trials' and directly below, in smaller font, it stated 'Tap to explore the dolutegravir (DTG) data'. To the left of the heading was a circle that stated 'Powered by DTG at the core'. Below this were three large circles which were labelled: GEMINI-1 and GEMINI-2 data, SWORD-1 and SWORD-2 data, and depth and breadth of DTG clinical trials. When the circles were accessed, further information about the studies was provided, including that the GEMINI and SWORD studies were non-inferiority studies and evaluated DTG as part of a 2-drug regimen and that 10 studies, including superiority and non-inferiority studies, evaluated DTG as part of a 3-drug regimen.

That Panel considered that the first screen of the interactive stand panel needed to stand alone as not all individuals would stop to click through the screens and read the supporting information.

The Panel noted ViiV's submission that in every phase 3, head to head study that DTG had been included in, the results had either shown DTG based regimens to be superior or non-inferior in comparison with regimens based on other ARVs and that no combination of ARVs had shown superiority over a DTG-based regimen in any head-to-head clinical trial in any patient population.

In the Panel view, the word 'unbeaten' would imply to the audience that DTG was unsurpassed in any head-to head clinical trials and not necessarily that it had superior efficacy or had surpassed its comparators.

The Panel noted that the interactive screens on the stand panel predominantly referred to DTG-based 2-drug regimens which were evaluated in non-inferiority studies (SWORD-1, SWORD-2, GEMINI-1 and GEMINI-2). In the Panel's view, non-inferiority studies evaluated whether one treatment was non-inferior to another treatment by a pre-specified margin. In this regard, the Panel queried the use of 'unbeaten' in the claim given that the material predominantly referred to DTG-based 2-drug regimens which were only supported by non-inferiority studies. This was reinforced by the layout and reading left to right would mean viewing the non-inferiority data first. Context was important. The Panel considered that the claim on the stand panel in question which was immediately followed by 'Tap to explore the dolutegravir (DTG) data' encompassed all DTG clinical trials, including DTG-based 3-drug regimens which had been evaluated in both superiority and non-inferiority studies. The Panel therefore considered the body of evidence for the claim ie both 2-drug and 3-drug DTG based regimens noting that there were a number of studies.

The Panel noted that Gilead had provided no evidence to suggest that there were ARV combinations that had surpassed either a 2-drug or a 3-drug DTG-based regimen in any head-to-head clinical trial.

The Panel noted Gilead's assertation that the screen with the claim in question did not adequately specify the restricted populations in the SWORD and GEMINI studies. The Panel noted that the screen in question contained no details of the patient populations in the studies and a user would have to click on the screen to access such information. In the Panel's view, this was not necessarily unacceptable provided that the information on the screen in question was not misleading. The Panel noted that both the Tivicay and the Juluca SPCs stated that these medicines should be prescribed by physicians experienced in the management of HIV infection. The Panel noted ViiV's submission that it was inconceivable that an expert HIV physician viewing the claim would assume that all the studies referred to identical patient populations.

The Panel noted its comments above and considered that although the claim 'Unbeaten in head to head clinical trials' was a strong, broad claim, there appeared to be data to support it and the audience would not be misled. Gilead had not shown, on the balance of probabilities, that the claim on the stand panel in question was ambiguous, misleading or incapable of substantiation as alleged and the Panel therefore ruled no breach of Clauses 7.2, 7.3 and 7.4.

The Panel did not consider that ViiV had failed to maintain high standards in this regard and ruled no breach of Clause 9.1.

**Complaint received** **26 February 2019**

**Case completed** **16 September 2019**

**CASE AUTH/3166/2/19**

# COMPLAINANT v SANOFI

## Alleged promotion of Epilim on Twitter

**A complainant who described him/herself as a concerned UK health professional, complained about a tweet sent by Sanofi UK. The tweet referred to Epilim (sodium valproate) and read:**

> **'Today we spoke @IMMDSReview [the Independent Medicines and Medical Devices Safety Review]. We have fully engaged in assisting the Review team to consider the complex issue arising from the use of Epilim to treat women and girls of child-bearing potential suffering from epilepsy.'**

**Epilim was indicated for the treatment of generalized, partial or other epilepsy. The summary of product characteristics (SPC) stated that for female children and women of childbearing potential, valproate must be initiated and supervised by a specialist experienced in the management of epilepsy. Valproate should not be used in female children and women of childbearing potential unless other treatments were ineffective or not tolerated. Further information was provided in a number of sections of the SPC including that every effort should be made to switch female children to alternative treatment before they reached adulthood.**

**The complainant noted that Epilim (sodium valproate) had a black triangle. The tweet included the brand name and the indication which was likely to attract interest in the use of Epilim in patients. The complainant alleged that as this was a promotional item sent out by the official Sanofi Twitter account, it was quite a serious matter and Clauses 2 and others needed to be addressed. The complainant noted that Twitter reached massive audiences extremely quickly and had the ability to do vastly more damage than traditional advertisements in medical journals and yet it appeared that much less care was taken.**

**The detailed response from Sanofi is given below.**

**The Panel noted Sanofi's submission that the tweet at issue contained material of general public interest; in the Panel's view, it was highly likely that Sanofi's Twitter followers would include members of the public. The Panel further noted that the nature of Twitter was such that tweets could be broadly and quickly disseminated in the public domain. When material was available to the public it needed to comply with the relevant requirements of the Code. Members of the public would include health professionals. There was no submission from Sanofi that the tweet was restricted in any way.**

**In the Panel's view, the tweet was not intended as advertising for a health professional audience and therefore the allegations relating to the promotion to health professionals were not relevant. The Panel ruled no breach in relation to these allegations. The Panel considered that as a general matter it was not necessarily a breach of the Code to tweet information to the public and some people would be interested in the ongoing safety review. The complainant had not provided any information to show that the public would not be interested in the information. Conversely, Sanofi submitted that the review had been established to examine concerns raised by patients and families, ie the public. The Panel considered all the circumstances including that the complainant had not met the burden of proving his/her complaint on the balance of probabilities in this regard and ruled no breach.**

**The Panel did not consider that the tweet amounted to disguised promotion. The company name, the name of the medicine and its indication were given. In the Panel's view, the general public would not be misled into thinking the nature of the tweet was disguised. This requirement was generally relevant when material for health professionals was disguised promotional material. The Panel ruled no breach of the Code.**

**In relation to the allegations about certification, the Panel considered that the tweet should have been certified. It related to a medicine and was intended for the public and a breach was ruled. The Panel ruled no breach in relation to the requirement to certify promotional material for health professionals.**

**The Panel noted the submission from Sanofi regarding its arrangements for training. In the Panel's view, the ruling of a breach of the Code did not in itself mean that a company had not met the training requirements. The Panel considered that the complainant had not proved, on the balance of probabilities, that a breach had occurred.**

**The Panel was concerned that the tweet did not explain that the review related to the adverse effects of sodium valproate – of which Epilim was one brand. Nor did the tweet reflect the important safety information in the current Epilim SPC regarding the cautions for the use of valproate in female children and women of childbearing potential. No explanation was given of the 'complex issue arising' from the use of Epilim in that patient group. Some readers might be left with the impression that there were no restrictions on the use of Epilim; insufficient information was provided in order for readers to understand the significance of, and the reason for, the review. In the Panel's view, the tweet did not give a balanced view and, in that regard, was misleading about the ongoing safety review and the use of the medicine; it might raise unfounded hopes of successful treatment. The Panel therefore ruled a breach of**

**the Code. The Panel noted that the complainant raised a general point about safety, referring to the use of the black triangle. The Panel considered that its ruling of a breach covered the general allegation referring to the use of the black triangle.**

**The Panel noted that the tweet named a prescription only medicine (Epilim) and referred to its use (in epilepsy). In that regard, the Panel considered that, on balance, a prescription only medicine had been advertised to the public and ruled a breach of the Code.**

**The Panel also ruled a breach as high standards had not been maintained.**

**The Panel noted that the tweet linked to @IMMDSReview. It considered that it would be clear to readers that this was the IMMDS Review Twitter handle and not a Sanofi site. The Panel therefore ruled no breach of the requirement to be clear when leaving a company site.**

**The Panel noted its rulings and comments above but did not consider that the particular circumstances of this case were such as to warrant a breach of Clause 2 which was a sign of particular censure.**

A complainant who described him/herself as a concerned UK health professional, complained about a tweet sent by Sanofi UK. The tweet referred to Epilim (sodium valproate) and read:

> 'Today we spoke @IMMDSReview [the Independent Medicines and Medical Devices Safety Review]. We have fully engaged in assisting the Review team to consider the complex issue arising from the use of Epilim to treat women and girls of child-bearing potential suffering from epilepsy.'

Epilim was indicated for the treatment of generalized, partial or other epilepsy. The summary of product characteristics (SPC) stated that for female children and women of childbearing potential, valproate must be initiated and supervised by a specialist experienced in the management of epilepsy. Valproate should not be used in female children and women of childbearing potential unless other treatments were ineffective or not tolerated. Further information was provided in a number of sections of the SPC including Section 4.3 Contraindications, Section 4.4, Special warnings and precautions for use where detailed information was provided about the use of the medicine in females including details of the pregnancy prevention programme and Section 4.6 Fertility, pregnancy and lactation. The SPC stated that prescribers must ensure that every effort should be made to switch female children to alternative treatment before they reached adulthood.

**COMPLAINT**

The complainant noted that Epilim (sodium valproate) had a black triangle. The tweet included the brand name and the indication which was likely to attract interest in the use of Epilim in patients. The complainant alleged that as this was a promotional item sent out by the official Sanofi Twitter account, it was quite a serious matter and Clauses 2, 4.1, 4.2, 4.3, 4.4, 4.9, 9.1, 9.9, 11.1, 12.1, 14.1, 14.5, 16.1, 26.1, 26.2, 28.1 and 28.6 needed to be addressed. The complainant acknowledged that this was a long list of clauses but unless they were mentioned they could not be reviewed by the Panel. The complainant noted that Twitter reached massive audiences extremely quickly and had the ability to do vastly more damage than traditional advertisements in medical journals and yet it appeared that much less care was taken.

Sanofi was advised that the complaint would be considered under the 2019 Code.

**RESPONSE**

Sanofi noted that the complaint was sent by email on 27 February 2019 and referred to a tweet published on Sanofi UK's Twitter account on 18 January 2019. The tweet reported on Sanofi's co-operation with the Independent Medicines and Medical Devices Safety (IMMDS) Review, directed by the Secretary of State for Health and Social Care and chaired by Baroness Cumberlege.

The IMMDS Review was a parliamentary review established to consider concerns raised by patients and families about three medical interventions, including sodium valproate, supplied as Epilim by Sanofi UK and as various different brands by other companies. The review's consideration of sodium valproate focussed on its use, principally as a treatment for epilepsy, in women and girls of child-bearing potential in view of the association with congenital malformations and developmental abnormalities in children exposed in utero.

Sanofi had provided substantial written material to assist the review in its consideration of sodium valproate in general and, in circumstances where Sanofi had knowledge only of its own product, Epilim in particular. On 18 January 2019, four Sanofi representatives provided oral evidence to the review and answered questions specifically about the supply of Epilim in the UK, the information provided in the product information for Epilim and the risk minimisation activities and materials directed and approved by the regulatory authorities and distributed by Sanofi UK.

The tweet at issue was published after the Sanofi representatives had appeared before the review. The public importance of the review and the public interest in the co-operation of relevant stakeholders with its work in the context of patient safety required no explanation. The tweet was issued in this context to confirm Sanofi's commitment to assisting the review in its consideration of these difficult issues. There was no intent to promote Epilim and the tweet did not do so. Sanofi submitted that the complaint was based on the incorrect premise that the tweet was promotional.

Clause 1.2 stated that promotion did not include various activities and material including:

- Factual, accurate, informative announcements and reference material concerning licensed medicines … provide they include no product claims;
- Summaries of product characteristics;
- Risk minimisation material; and
- The labelling on medicines and accompanying package leaflets insofar as they are not promotional for the medicines concerned ….'

Sanofi submitted that the tweet in question was a factual, informative announcement on a matter of public interest. Sanofi noted that the complainant claimed that there were two references in the tweet, which he/she seemingly construed demonstrated a promotional intent: (i) an indication for use; and (ii) use of the brand name. However, both of these elements were required for useful communication about a matter of public importance and did not, in the particular circumstances of the tweet, constitute promotion:

i. The reference to treatment of women and girls of child-bearing potential did not promote the use of Epilim in this patient population, but instead highlighted the difficulties of therapy in this patient group. The wording reflected and explained the purpose of the review and why Sanofi had been asked to give oral evidence on its product and the information provided in the product information for Epilim (and not the other generic sodium valproate products).

ii. Use of a brand name did not establish a promotional intent. In this case, the use of the brand name in the tweet was appropriate and non-promotional, because the announcement described Sanofi's co-operation with the review and the evidence it gave during the oral hearing, in circumstances where Sanofi's evidence focused upon the supply of Epilim and the development of information provided with Epilim, rather than generic sodium valproate.

In circumstances where the tweet was non-promotional, the substance of the complaint fell away and most of the identified clauses of the Code were not applicable.

Sanofi noted that Clauses 4.1, 4.2, 4.3, 4.4 and 4.9 addressed requirements for supply of prescribing information, non-proprietary name and an adverse event statement in all promotional material. Sanofi submitted that for the reasons explained above, the tweet was not promotional and the identified provisions did not apply and were not breached.

Sanofi stated that the messages on its Twitter account were seen only by those who had communicated a positive decision to 'follow' Sanofi or who otherwise elected to access the account. The tweet at issue contained material of general public interest.

For the reasons explained above, Sanofi stated that the tweet was non-promotional and fell outside the scope of the Code. There was no breach of Clause 11.1. As the tweet was not promotional and could not, therefore, be characterised as disguised promotion, there was no breach of Clause 12.1.

Sanofi stated that its social media policy required that all content of social media channels (including tweets) was approved in accordance with appropriate Code requirements, applicable policies and standard operating procedures (SOPs). However, as the tweet was non-promotional and did not fall within the scope of Clause 14.1 or the non-promotional activities identified in Clause 14.3, there was no requirement to certify it in accordance with Clause 14 and the complainant had provided no evidence to indicate a breach of Clause 14.1 or Clause 14.3.

The social media policy also provided that the content of all social media channels (including Sanofi UK's Twitter account) was the responsibility of the relevant channel owner, who had to ensure that appropriate approval procedures were followed. All Sanofi UK social media accounts were password controlled and content could be added only by authenticated users.

Sanofi explained that its training requirements in relation to the Code were set out in a policy. All Sanofi personnel were required to be trained on the general principles of the Code, repeated annually, and to demonstrate competence by achieving a satisfactory score in their responses to mandatory questions. More senior staff, including all of those concerned in any way with the preparation of material or activities covered by the Code were required to participate in and pass comprehensive in-house training on the relevant legal requirements and Code provisions. This training incorporated the requirements for promotion via electronic methods and social media. Following the initial programme, continuing training was undertaken to ensure that competence was maintained and updated.

The information in the tweet at issue related only indirectly to prescription only medicines; it was principally focussed on the independent review directed by Government. To the extent that it did constitute information 'about' prescription only medicines, it fell within the description of 'factual and balanced' material of public interest. The tweet was non-promotional and clearly did not encourage members of the public to request a specific prescription only medicine; rather it highlighted Sanofi's co-operation with the consideration of safety-related concerns raised by patients. Sanofi denied a breach of Clauses 26.1 or 26.2.

Sanofi reiterated that the tweet was non-promotional and was not subject to the Code. There was accordingly no breach of Clause 28.1 and the complainant had provided no evidence suggesting otherwise. The reference to Clause 28.6 was not understood. The tweet was published on a Sanofi sponsored Twitter account and included no link to any other site.

Sanofi submitted that the tweet notified followers of its Twitter account and those who chose to access the account of a factual matter of public importance. The tweet fell outside the scope of the Code.

In these circumstances, there was no basis for any finding that Sanofi had not maintained high standards. Sanofi stated that it had not breached relevant provisions of the Code, comprehensive policies were in place, and were followed and these policies were regularly updated and monitored in order to ensure that the company did not fall below standards required by the applicable legislation and the Code. Sanofi denied a breach of Clause 9.1.

Sanofi stated that as explained above, the tweet did not constitute an activity or material associated with promotion and fell outside the scope of the Code; the company denied a breach of Clause 2.

Sanofi stated in conclusion that the complaint was based on the incorrect assumption that the tweet was promotional; it was instead a non-promotional, factual announcement on a matter of public interest and therefore it fell outside the scope of the Code. In these circumstances, the clauses of the Code cited by the complainant were irrelevant and/or the complainant had submitted no evidence of breach.

**PANEL RULING**

The Panel noted that the use of social media including Twitter to provide information to the public was a legitimate activity for pharmaceutical companies as long as the material complied with the Code, particularly Clause 26.

The Panel noted Sanofi's submission that the tweet at issue contained material of general public interest; in the Panel's view, it was highly likely that Sanofi's Twitter followers would include members of the public. The Panel further noted that the nature of Twitter was such that tweets could be broadly and quickly disseminated in the public domain. When material was available to the public it needed to comply with the relevant requirements of the Code. Members of the public would include health professionals. There was no submission from Sanofi that the tweet was restricted in any way.

In the Panel's view, the tweet was not intended as advertising for a health professional audience. The Panel therefore considered that the allegations relating to the promotion to health professionals were not relevant. The Panel ruled no breach of Clauses 4.1, 4.2, 4.3, 4.4, and 4.9 of the Code. Similarly, the need to obtain prior permission before sending out the tweet did not apply to material for the public and no breach of Clause 9.9 was ruled.

The Panel considered that as a general matter it was not necessarily a breach of the Code to tweet information to the public and some people would be interested in the ongoing safety review. The complainant had not provided any information to show that the public would not be interested in the information. Conversely, Sanofi submitted that the review had been established to examine concerns raised by patients and families, ie the public. The Panel considered all the circumstances including that the complainant had not met the burden of proving his/her complaint on the balance of probabilities in this regard. The Panel ruled no breach of Clause 11.1.

The Panel did not consider that the tweet amounted to disguised promotion. The company name, the name of the medicine and its indication were given. In the Panel's view, the general public would not be misled into thinking the nature of the tweet was disguised. This requirement was generally relevant when material for health professionals was disguised promotional material. The Panel ruled no breach of Clause 12.1.

In relation to the allegations about certification, the Panel considered that the tweet should have been certified. It related to a medicine and was intended for the public. Certification of material for the public was covered by Clause 14.3. The company acknowledged that the tweet had not been certified. Sanofi had not met the requirements of Clause 14.5 as alleged and a breach was ruled by the Panel. The Panel ruled no breach of Clause 14.1 as the tweet was not promotional material for health professionals.

The complainant had not provided any detail or evidence regarding the alleged breach of Clause 16.1. The Panel noted the submission from Sanofi regarding its arrangements for training staff. In the Panel's view, the ruling of a breach of the Code did not in itself mean that a company had not met the training requirements set out in Clause 16.1. The Panel considered that the complainant had not proved, on the balance of probabilities, that a breach of Clause 16.1 had occurred and no breach was ruled.

The Panel was concerned that the tweet did not explain that the review related to the adverse effects of sodium valproate – of which Epilim was one brand. Nor did the tweet reflect the important safety information in the current Epilim SPC regarding the cautions for the use of valproate in female children and women of childbearing potential. No explanation was given of the 'complex issue arising' from the use of Epilim in that patient group. Some readers might be left with the impression that there were no restrictions on the use of Epilim; insufficient information was provided in order for readers to understand the significance of, and the reason for, the review. In the Panel's view, the tweet did not give a balanced view and, in that regard, was misleading about the ongoing safety review and the use of the medicine; it might raise unfounded hopes of successful treatment. The Panel therefore ruled a breach of Clause 26.2 of the Code. The Panel noted that the complainant raised a general point about safety, referring to the use of the black triangle. This was covered by Clause 26.3 in relation to material for patients taking the medicine. However, the tweet was not specifically for patients taking Epilim. The Panel considered the general allegation referring to the use of the black triangle was covered by its ruling of a breach of Clause 26.2.

The Panel noted that the tweet named a prescription only medicine (Epilim) and referred to its use (in epilepsy). In that regard, the Panel considered that, on balance, a prescription only medicine had been advertised to the public and ruled a breach of Clause 26.1 of the Code.

The Panel noted its rulings above and considered that high standards had not been maintained. It therefore ruled a breach of Clause 9.1 of the Code.

The Panel noted that Clause 28.1 stated that promotional material about prescription only medicines directed to a UK audience which is provided on the Internet must comply with all relevant requirements of the Code. The Panel ruled no breach of this clause given its decision that the material was for the public as set out in its rulings of breaches of Clauses 26.1 and 26.2 above.

The Panel noted that Clause 28.6 stated that it should be made clear when a user was leaving any of the company's sites, or sites sponsored by the company, or was being directed to a site which was not that of the company. The Panel noted that the tweet linked to @IMMDSReview. It considered that it would be clear to readers that this was the IMMDS Review Twitter handle and not a Sanofi site. The Panel therefore ruled no breach of Clause 28.6.

The Panel noted its rulings and comments above but did not consider that the particular circumstances of this case were such as to warrant a breach of Clause 2 which was a sign of particular censure. No breach of Clause 2 was ruled.

**Complaint received** **27 February 2019**

**Case completed** **11 June 2019**

# COMPLAINANT/DIRECTOR v NOVARTIS

## Use of Twitter/alleged breach of undertaking

**A complainant, who described him/herself as a concerned UK health professional, complained about a retweet from Novartis which had appeared in his/her Twitter feed. The tweet, originally sent by a clinician who had attended a Novartis meeting, read:**

> **'So many terrific talks at the @NovartisUK Haematology Masterclass meeting on recent advances in MPN, AML, CAR, ITP, AA, CML (attached pic of [name] giving an excellent plenary talk) and many more. Haematology is such an exciting field – can't wait for next year!!'**

**The complainant searched on line as he/she did not know what the Novartis Haematology Masterclass was and found the website for the Association of Myeloid Neoplasm Practitioners (AMNP) with a Haematology Academy flyer. This was the first mention that the meeting was promotional. Novartis had thus retweeted a health professional's tweet about a Novartis' promotional meeting – the complainant alleged that this was disguised promotion as well as promotion to the public.**

**The complainant noted a statement on the AMNP website: 'Developed with support from Novartis Pharmaceuticals UK Ltd'. The complainant alleged that this lacked clarity as to the relationship between Novartis and the AMNP. The website appeared to only promote Novartis meetings and host Novartis' promotional content. This ranged from an act unilaterally undertaken by the AMNP to one that was actively aided by Novartis to do so.**

**The complainant stated that the Haematology Academy flyer had no prescribing information.**

**The complainant stated that a few months previously, a Novartis employee was found to have promoted to the public [Case AUTH/3038/4/18] and now the official Novartis UK Twitter feed had done almost the same thing. The complainant stated that this hardly demonstrated that any lessons were learned and suggested that the undertaking given in the previous case be reviewed.**

**In relation to the alleged breach of undertaking, this aspect would proceed in the name of the Director.**

**The detailed response from Novartis is given below.**

**The Panel noted that Novartis UK had retweeted, without any additional comment, a tweet posted by a health professional who had attended a Novartis promotional meeting. The Panel agreed that there was potentially a difference between sharing information about the content of a meeting and sharing information about the arrangements. It was important that those attending meetings were clear about the content of such meetings as well as the role of pharmaceutical companies in the arrangements.**

**The Panel noted that the tweet did not contain links to other sites but had included the Novartis UK Twitter handle. The tweet referred to recent advances in MNP [myeloproliferative neoplasms], AML [acute myeloid leukaemia], CAR [chimeric antigen receptor], ITP [immune thrombocytopenia], AA [aplastic anaemia] and CML [chronic myeloid leukaemia] and included a picture of a speaker and part of a PowerPoint slide. The Panel noted that no specific medicine was directly mentioned in the text of the tweet and, in its view, no medicine was legible from the slide in the picture within the tweet.**

**In the Panel's view, as the tweet made no direct or indirect reference to a specific medicine, it did not consider that Novartis' retweet constituted promotion of a prescription only medicine to the public and ruled no breach of the Code.**

**The Panel noted the allegation of breach of undertaking and that the complainant had referred to Case AUTH/3038/4/18. In that case, a Novartis employee had disseminated information referring to a prescription only medicine to contacts in his/her personal LinkedIn account and the company was found to be in breach of the Code including advertising to the public. The Panel noted that a form of undertaking and assurance was an important document. Companies had to give an undertaking that the material in question and any similar material, if not already discontinued or no longer in use, would cease forthwith and give an assurance that all possible steps would be taken to avoid similar breaches of the Code in future. The Panel noted that although both cases related to the alleged promotion of a prescription only medicine to the public via a social media channel, there were differences. The Panel noted, however, its ruling above of no breach and thus ruled no breach of the Code including Clause 2 in relation to the allegation of a breach of undertaking in Case AUTH/3038/4/18.**

**The Panel did not consider that the retweet constituted disguised promotion and ruled no breach of the Code.**

**The Panel noted that the Novartis haematology academy flyer contained the Novartis logo and a website address for the haematology academy; it invited readers to register for future haematology events and access past meeting material. It also stated, 'Discover a growing collection of Novartis educational content and materials, easily accessible on one platform'. At the bottom of the flyer, it stated: 'Events are either organised or sponsored by Novartis Pharmaceuticals UK Ltd.' and 'This website [haematology academy] has been developed**

**by Novartis Pharmaceuticals UK Ltd for use by HCPs [healthcare professionals] only and contains promotional material'. The Panel noted Novartis' submission that there was no active hyperlink to the haematology academy contained within the flyer and that if users typed in the URL address, or found it by an internet search, they would have to declare they were a health professional and register as the website was access restricted.**

**The Panel noted that the flyer at issue contained no direct or indirect reference to a specific medicine and therefore, in its view, did not require prescribing information. No breach of the Code was ruled.**

**The Panel considered that the AMNP website declaration 'Developed with support from Novartis Pharmaceuticals UK Ltd' could have been clearer given Novartis was also providing support to AMNP for the website's ongoing maintenance; particularly as another company was listed as providing support for the website maintenance. The AMNP website had a Novartis flyer for the haematology academy which Novartis submitted was uploaded following a decision by the AMNP steering group and without Novartis' involvement or influence. The Panel noted Novartis' submission that it did not have any influence over the AMNP, its website or the materials hosted upon it and it had no involvement in the flyer being made available on the AMNP website.**

**The Panel considered that, on balance, the declaration was not misleading as to the relationship between Novartis and the AMNP in relation to the website content where it appeared Novartis had no influence. The Panel therefore ruled no breach based on the narrow allegation.**

**The Panel noted its comments above and did not consider that Novartis had failed to maintain high standards and ruled no breach of the Code.**

A complainant, who described him/herself as a concerned UK health professional, complained about a retweet from Novartis which had appeared in his/her Twitter feed. The tweet, originally sent by a clinician who had attended a Novartis meeting, read:

> 'So many terrific talks at the @NovartisUK Haematology Masterclass meeting on recent advances in MPN, AML, CAR, ITP, AA, CML (attached pic of [name] giving an excellent plenary talk) and many more. Haematology is such an exciting field – can't wait for next year!!'

**COMPLAINT**

The complainant stated that he/she did not know what the Novartis Haematology Masterclass was so he/she searched for it online and found the website for the Association of Myeloid Neoplasm Practitioners (AMNP) with a Haematology Academy flyer. This was the first mention that the meeting was promotional. Novartis had thus retweeted a health professional's tweet about Novartis' own promotional meeting – the complainant alleged that this was disguised promotion as well as promotion to the public.

The complainant did not know what the relationship between the AMNP website and Novartis was, although he/she noted a statement on the website: 'Developed with support from Novartis Pharmaceuticals UK Ltd'. The complainant alleged that this lacked clarity as to the relationship between Novartis and the AMNP. The complainant stated that he/she did not know the contractual arrangement between the two but the AMNP website appeared to only promote Novartis meetings and host Novartis promotional content. This ranged from an act unilaterally undertaken by the AMNP to one that was actively aided by Novartis to do so.

The complainant provided a copy of the Haematology Academy flyer and stated that it had no prescribing information nor a link to such.

The complainant stated that a few months previously, a Novartis employee was found to have promoted to the public [Case AUTH/3038/4/18] and now, after case completion and remedial action apparently taken, the official Novartis UK Twitter feed had done almost the same thing. The complainant stated that this hardly demonstrated that any lessons were learned and suggested that the undertaking given in the previous case be reviewed.

When writing to Novartis, the Authority asked it to consider the requirements of Clauses 4.1, 9.1, 9.10, 12.1 and 26.1 of the 2019 Code. In relation to the alleged breach of undertaking, this aspect would proceed in the name of the Director and Novartis was asked to consider the requirements of Clauses 2 and 29.

**RESPONSE**

Novartis submitted that the retweet did not constitute direct-to-consumer promotion or disguised promotion and was most unlikely to lead to a consumer asking for a particular medicine. The retweet was never intended to promote a prescription-only product, nor could it have that effect based on an objective and reasonable analysis of the content. Rather, the retweet drew attention to the fact that a clinician valued attending a health professional only event. It was a key corporate aim to contribute to scientific education and provide value to the healthcare community and the purpose of the retweet was simply to highlight this and show that it was appreciated by attendees. Neither the retweet nor the event itself were about a particular Novartis product and the company did not accept that the retweet had a product promotional purpose. It was appropriate, and commonplace, for pharmaceutical companies to share on social media comments and other news that supported their wider corporate goals and educational activities, particularly when that was about unbranded, non-product-specific meetings and events that had an educational focus. The fact that the meeting might also have included some promotional content did not alter that principle – sharing information about the meeting was clearly distinguishable from sharing the promotional content of the meeting. If that were not the case, it would mean that a pharmaceutical company could not mention on any public forum the fact that it held a promotional or educational

meeting as even this would be deemed product promotion. Such an approach would run contrary to established principles in medicines advertising law, regulation, and also prior approaches taken by the PMCPA. Moreover, this approach would fundamentally alter the way in which pharmaceutical companies communicated over social media and it would ultimately undermine the industry's efforts to build trust and engage with the public. Novartis stated that it worked hard to build value for the healthcare community and was committed to being open and transparent about how it engaged with health professionals and the NHS.

In that context, Novartis stated that it was disappointed that the complainant conflated the two issues in a way that was unsupported by the facts and the Code. The complainant stated that having read the retweet, he/she researched the Haematology Masterclass and this led him/her to the AMNP website which contained a 2018 information flyer for the Haematology Academy. The flyer stated that the Haematology Academy ran events that Novartis organized/sponsored and that its website contained health professional only information developed by Novartis, which might contain promotional material. None of those websites or links were product promotional, and product promotional material on the Haematology Academy website was access restricted to registered health professionals. The complainant had clearly gone to some lengths to try and establish a link between the retweet and the promotion of Novartis' products; Novartis noted that he/she had been unable to do so. This again went to the core of the issue – that a tweet about an event run by a pharmaceutical company (even if the event was promotional) was clearly separate from a communication about the content of that event and/or the promotion of a product. That separation was self-evident from the complaint – the complainant did not allege that the retweet promoted a product precisely because that was not the impression anyone would get from viewing it. Put simply, the retweet did not lead lay viewers to become interested in a Novartis product and asking their healthcare providers to prescribe it.

Novartis submitted that in light of the above, it was clear that the retweet was a non-product-promotional communication and hence there had been no breach of Clauses 4.1, 12.1 or 26.1. The retweet and the contents of the flyer were entirely appropriate in the circumstances as non-promotional information about an event, and unrelated to any medicine or specific diseases. It followed that there was no breach of Clause 9.10. High standards had been maintained and Novartis did not see any grounds for a breach of Clause 9.1.

Given the above, Novartis did not see how it had breached the undertaking given in Case AUTH/3038/4/18. That case concerned the company guiding its employees about their use of personal social media accounts. Although there was a similar medium here, this case concerned the extent to which the company itself could engage in non-promotional communications over social media. The two were markedly different in that respect and Novartis did not see how that would affect the undertakings, which it gave sincerely and in good faith. Therefore, Novartis did not see the basis for alleging breaches of Clauses 2 and 29 of the Code.

**Original tweet**

Novartis explained that on 15 February 2019 it held the 'Haematology Masterclass', an annual health professional only educational meeting; it was attended by over 250 attendees and had CPD accreditation. There were over 25 speakers from the UK and overseas, with the programme put together by Novartis and an external faculty of medical experts. The main focus of the meeting was education but there were some promotional elements and so for transparency purposes Novartis treated the event as a promotional meeting.

On the same day, a clinician who attended the masterclass posted the original tweet on his personal Twitter account about the positive experience he had at the meeting and how he was excited for next year. Novartis noted that the tweet was posted in the evening after the event had concluded. The clinician complimented one of the speakers on 'giving an excellent plenary talk' and included a picture of that speaker presenting. The text of the original tweet mentioned the disease areas covered in the programme and clearly acknowledged that this was a Novartis organised event. The name of the event, 'Haematology Masterclass' featured prominently in the background of the picture, without featuring Novartis' name or logos. There was no suggestion whatsoever in the original tweet that its purpose was to promote a specific product.

Although not mentioned by the complainant, Novartis noted that if the picture accompanying the tweet was significantly enlarged, it was possible on the top left to see part of one of the slides the speaker was presenting when the picture was taken. At the top of the slide it was possible to discern the name 'imatinib', which was the non-proprietary name for Glivec, marketed by Novartis. Generic versions of Glivec were also available. Novartis stated that it had referred to this for the sake of absolute transparency and did not consider that this was a material element of the complaint. The text on the slides was purely incidental to the picture of the speaker and would be illegible when viewed in the Twitter app on a smartphone and barely legible on a computer. Some of the text became legible if blown up to an uncommonly large format, which Twitter users were highly unlikely to do and, it was clear, the complainant did not do.

Novartis noted that even if Twitter users expanded the picture to an unnaturally large size, they would see the non-proprietary name of the product alone, with no brand name, no product claims nor a reference to the product's indication (eg chronic myeloid leukaemia). The text of the original tweet did mention learning about 'MPN, AML, CAR, ITP, AA [and] CML' at the meeting. These were general references to the scientific programme and not indications of any product, including imatinib. Lay viewers of the picture and the original tweet would not know what imatinib was licensed for. Novartis did not understand how a purely incidental and

almost invisible non-proprietary name would have the effect of raising awareness of, or interest in, Glivec, particularly without any mention of a disease. The most obvious analogy was with reply paid cards, which could feature the name of a product (and, of course, prior to that so-called promotional aids which could bear the brand name of the medicine but not the indication). It was well established that such cards did not promote the product to people who viewed the cards in passing (eg postal workers) because there was no product claim and no reference to the licensed indication. The same principles clearly applied to this case: even if a member of the public were to blow up the picture to an unnatural size, the effect would not be to promote a product. Notwithstanding that, Novartis had instructed its social media team to pay particular attention to names or other details that were incidentally mentioned in pictures to reduce any ambiguity or potential confusion.

In conclusion, Novartis submitted that the original tweet related to the Haematology Masterclass and was not directly or indirectly about any Novartis product, nor did it contain any claim about a Novartis product. For these reasons, it was self-evident that the original tweet was not product promotional, was not posted for product promotional reasons, and under any reasonable assessment, did not have a product promotional effect.

**The retweet**

On 18 February 2019, days after the conclusion of the meeting, Novartis retweeted the original Twitter message on its Twitter account '@NovartisUK' without adding any further text or comment. The complainant's allegation was that the act of retweeting was somehow product promotional.

Retweets and liking/sharing content on social media had been the subject of a number of recent PMCPA cases and Novartis appreciated that the PMCPA was managing a media environment that raised a number of complex regulatory challenges. That said, it was well-established in this case history, wider principles and the unique facts of this case that the retweet did not have the purpose or effect of promoting Novartis' products. Reasons for this included:

- As noted in Case AUTH/3038/4/18, assessing whether social media activity amounted to promotion was nuanced and complex and required a case-by-case assessment. Novartis noted that the PMCPA had raised this point in other rulings about social media and had taken into account a range of factors including the nature of the material disseminated, its overall context and product references. It was important for the PMCPA to take a similarly holistic approach in this case and not simply conclude that any tweet by a pharmaceutical company was automatically product promotional.
- Particularly when pharmaceutical companies proactively disseminated information (eg by retweeting), it was a well-established principle of medicines advertising law that there should be an objective assessment of whether this was for promotional purposes. For example, the EU Court of Justice has held: 'the **purpose** of the message constitutes the **fundamental defining characteristic of advertising,** and **the decisive factor** for distinguishing advertising from mere information' (emphasis added). The Court continued: 'If the message is designed to promote the prescription, supply, sale or consumption of medicinal products, it is advertising …'. And further: 'The question whether a dissemination of information has a promotional objective must be determined by undertaking a detailed examination of all the relevant circumstances of the case …'.
- Under any reasonable interpretation, Novartis' retweet of the original tweet could not be said to be for product promotional purposes. Novartis did not add to or embellish the original tweet and it did not mention its product alongside the retweet. It was clear that the main purpose of the retweet was to demonstrate that a respected health professional valued attending a Novartis health professional only event and, by that, reaffirm Novartis' commitment to holding events that added value to the healthcare community. The original tweet did not draw attention to any of the promotional content of the meeting and it did not name specific Novartis products. The retweet was not intended to turn, and did not turn, the non-promotional original tweet into a promotional one.
- Companies had a legitimate right to communicate with health professionals and the public about meetings and events and there were several examples of pharmaceutical companies doing so. The PMCPA had in the past accepted that these communications would only come within the scope of the Code if they provided information about, or promoted, prescription-only medicines. For example, the PMCPA's Digital Guidelines stated: 'The use of social media to promote, increase awareness and encourage engagement with health professionals about prescription medicines is very likely to be seen as promotion …'. It followed that where there was no purpose to promote, increase awareness of or otherwise engage with health professionals about a product, social media activity would fall outside the concept of promotion.
- That was supported by a line of PMCPA cases. For example, the PMCPA had found companies in breach of the Code where their social media activities were about specific products. However, in other cases, tweets that did not mention and were unrelated to a product were not considered promotional. Crucially, in Case AUTH/2612/6/13 the PMCPA distinguished between tweets that were about a promotional meeting and made no reference to any particular products (which it deemed non-promotional per se); and tweets that mentioned the event, the name of the product and its licensed indication (which were deemed promotional). It was patently clear that the retweet in this case fell into the former category as it had no relationship with any Novartis product.
- From a broader industry perspective, Novartis stated that it had deep concerns about the nature of this complaint and the future direction of travel

for pharmaceutical companies which engaged in legitimate non-promotional communications on social media. Novartis, and no doubt other companies, would be deeply troubled if the outcome of this case was that companies could not raise awareness of the positive impact of its work in a non-promotional way, or of meetings and events when the communications in question had no direct or indirect link to communicating to the public about medicines, let alone promoting them. This would represent a significant shift in the PMCPA's historical position as understood by industry and have considerable repercussions and would seem to be an unreasonable and disproportionate step when the ultimate aim of regulation was to protect the public from inappropriate advertising. If the PMCPA was concerned about industry's understanding of these issues, it should issue or update its guidance in consultation with industry.

**Other documents/webpages mentioned in complaint**

Novartis stated that although not especially clear, the complainant mentioned that he/she did research into the 'Haematology Masterclass' and discovered that it was a promotional meeting linked to the Novartis funded Haematology Academy (whose access restricted health professional only website contained promotional and educational content). The complainant did not allege that any of these websites or materials contained publicly visible promotional content, but rather that this established a link to the meeting being promotional. As noted above, the meeting had a strong educational focus but because of certain promotional elements, Novartis regarded it as a promotional meeting. As such, the content of the meeting was certified in accordance with its standard certification procedures.

With regard to the organisations and documents referred to by the complainant, Novartis submitted the following:

**The Association of Myeloid Neoplasm Practitioners (AMNP)**

Novartis stated that the AMNP was a professional association founded in 2006 by myeloid neoplasm health professions to establish a professional network and support those caring for patients with myeloid neoplasms and other haematological conditions, particularly in clinic settings. This was achieved by hosting educational events, and publishing other events and resources relevant to this area. The AMNP was open to any health professional involved in the care of patients with myeloid neoplasm, but was composed predominantly of nurses and pharmacists, some of whom were prescribers and some who were not. Novartis had contributed to the establishment of the AMNP website by providing a grant. Novartis also ran an annual nurse meeting, which it classed as promotional.

**The Haematology Academy**

The Novartis Haematology Academy was a promotional website that had information on brands, meetings, etc. It was hosted on Novartis' health professional website; users had to log-in to declare that they were health professionals and register.

**The Haematology Academy Flyer on the AMNP's website**

The flyer raised awareness of the Haematology Academy website that contained Novartis' promotional initiatives in haematology. The flyer itself did not contain any visible promotional content, and clearly advised that the internal content of the Haematology Academy website was aimed at health professionals only and contained promotional materials. Novartis stated that out of an abundance of caution the flyer was certified in accordance with standard procedures.

Viewers could only access the promotional material referenced in the flyer by independently going onto the Haematology Academy website, either by typing the URL address found on the flyer or searching the internet for it. There was no active link to the Haematology Academy website contained in the flyer, as uploaded onto the AMNP's website. Once users reached the Haematology Academy website, they had to positively confirm their status as health professionals and, finally, enter correct log-in details. Neither the original tweet nor the retweet contained any link or direction to the flyer, or to the material referenced within it. It was only through his/her own research that the complainant located the flyer; it was not material that was advertised to the public in either tweet. As per the EU Court of Justice Merck Sharp & Dohme case (C-316/09) cited above, if such information sat passively on a platform and required active steps to search and find it, that was a key factor indicating that the information on the platform was not promotional. That was the situation in the Merck Sharp & Dohme case where the internet platform was fully open-access. In contrast, it was clear on the facts of this case that there were a number of steps in place to prevent those who were not health professionals from accessing the material concerned.

**Alleged breaches of the Code**

With regard to specific clauses of the Code, Novartis commented as follows:

**Clause 4.1** – It had already been established that the retweet and the flyer were non-product-promotional communications. The only promotional content on any ancillary website or document was behind health professional only access restrictions and prescribing information was available in that context. Novartis denied a breach of Clause 4.1.

**Clause 9.10** –The assessment of the retweet and the flyer did not change because the underlying event was promotional. The focus must be on the

communication itself. Nevertheless, it was clear from the content of the original tweet and the retweet that the Haematology Masterclass was sponsored by Novartis (this was shown in the text accompanying the picture). Novartis denied a breach of Clause 9.10.

**Clause 12** –The identity of Novartis as the event sponsor was clear in the original tweet and the retweet. Novartis did not make any effort to conceal its identity in the retweet, rather it reproduced, in full, a tweet from an individual that had attended a Novartis sponsored event. It could not be said that the flyer for the Haematology Academy was disguised promotion by Novartis. If members of the public followed the links on the AMNP website to access the flyer, they would see that it stated on its face that events were either organised or sponsored by Novartis, and that the website had been developed by the company for use by health professionals only and that it contained promotional material. Novartis denied a breach of Clause 12.

**Alleged breach of undertakings**

Novartis did not accept that it had breached the undertaking given in Case AUTH/3038/4/18. Novartis gave that undertaking solemnly and in good faith and took its compliance responsibilities very seriously. The company had taken a number of proactive steps to improve how its employees managed their social media accounts. These included:

- on 11 December 2018, a company-wide email from Novartis' country president which focussed on the lessons from the PMCPA ruling and what conduct Novartis considered acceptable for its associates when active on social media;
- a company-wide call the next day by the country president to reinforce to associates what acceptable conduct was when being active on social media; and
- after receiving the complaint, before the case was decided and before the undertaking was entered, Novartis developed a local UK policy for personal use of social media and related training, which was rolled out from July 2018 onwards. Such training was now provided as core training to all new joiners.

Notwithstanding the above, the current case concerned a materially different point. Case AUTH/3038/4/18 was about giving appropriate guidance to employees about their use of social media. By contrast, the current case concerned the boundaries of legitimate non-promotional communication from a recognised company social media account and where the retweeting had been approved through a specific company procedure. Novartis provided a copy of the procedure which, in summary, permitted using Novartis social media accounts to engage with non-company content (eg retweeting) provided that there was no relationship with the company's products and was non-contentious. Novartis was confident that this was the correct approach and was consistent with PMCPA guidelines and the law. The company was also confident that the correct procedures were followed in this case, however, it had reminded colleagues to pay particular attention to all images (including out-of-focus images) in case they mentioned a specific product to avoid any confusion or ambiguity on this point. Further, the two cases also concerned two entirely different sets of policies: the first related to an employee social media policy; the second to a communications strategy.

Given the above, Novartis denied a breach of undertaking; the current case did not involve a breach of the Code and, even if the PMCPA were to rule against Novartis, the breaches were materially different to the subject matter of the undertakings. Novartis thus denied a breach of Clause 29 and of Clause 2.

Following a request for further information, Novartis submitted that it did not have any influence over the AMNP, their website or the materials hosted upon it. Novartis had contributed to the establishment and the maintenance of the AMNP website by providing two separate grants:

- provision of funds (£15915) for the establishment of the website in May 2016;
- contribution, alongside another pharmaceutical company, for half the cost of maintenance and hosting of the AMNP website for a period of three years, in June 2018, amounting to £2202 (£4404 total cost).

Novartis submitted that, in compliance with its internal guidelines and the Code, the grants were provided following unsolicited requests; no benefits were received by Novartis in return and disclosure of the relative transfers of value had been and would be made, respectively, as applicable.

Novartis stated that the Haematology Academy leavepiece was certified for hard copy distribution to health professionals and only hard copies were printed. No electronic copies were distributed or disseminated; from the posting on the AMNP website the imagery and text appeared consistent with a hard copy being scanned and uploaded. The membership of AMNP was made up of health professionals and Novartis' assumption was that one of them scanned the leavepiece and uploaded it to their website.

Novartis submitted that it contacted the AMNP steering committee (copy of correspondence provided) which, through one of its members, confirmed the independence of the AMNP when deciding what to upload to the website and the circumstances surrounding the upload of the leavepiece to the AMNP website. Novartis quoted from the AMNP's response that the AMNP 'look for material that might be of use, and […] the AMNP steering group decide what to upload to the website' and that the leavepiece 'was acquired by an individual registered user of the AMNP website for personal use. It is likely that it was picked up at a recent meeting. The registered users of the AMNP website are health care professionals, which are also the intended users of the Novartis Haematology Academy. The leaflet was scanned onto the website'.

**PANEL RULING**

The Panel noted that the use of social media, including Twitter, to provide information to the public was a legitimate activity if the material complied with the Code. Each case needed to be considered on its own particular merits. When a health professional tweeted material from a pharmaceutical company meeting, that material was not necessarily covered by the Code. Much would depend on the relationship between the pharmaceutical company and the health professional. However, when a pharmaceutical company circulated that material eg by retweeting it, then that material was potentially subject to the Code, even if the company had not altered the material in any way.

The Panel noted that Novartis UK had retweeted, without any additional comment, a tweet posted by a health professional who had attended a Novartis promotional meeting. The Panel noted that the Code required every meeting to have clear educational content and this applied to meetings where medicines were promoted. The Panel agreed that there was potentially a difference between sharing information about the content of a meeting and sharing information about the arrangements. It was important that those attending meetings were clear about the content of such meetings as well as the role of pharmaceutical companies in the arrangements.

The Panel noted that the tweet did not contain links to other sites but had included the Novartis UK Twitter handle. The Panel noted that the tweet at issue referred to recent advances in MNP [myeloproliferative neoplasms], AML [acute myeloid leukaemia], CAR [chimeric antigen receptor], ITP [immune thrombocytopenia], AA [aplastic anaemia] and CML [chronic myeloid leukaemia] and included a picture of a speaker and part of a PowerPoint slide. The Panel noted that no specific medicine was directly mentioned in the text of the tweet and, in its view, no medicine was legible from the slide in the picture within the tweet. The Panel considered, however, that particular care must be taken if a company's medicine, even though not named, was the only medicine associated with a certain disease or mechanism of action etc. Novartis made no submission in this regard.

In the Panel's view, as the tweet made no direct or indirect reference to a specific medicine, it did not consider that Novartis' retweet constituted promotion of a prescription only medicine to the public and ruled no breach of Clause 26.1.

The Panel noted the allegation of breach of undertaking and that the complainant had referred to Case AUTH/3038/4/18. In Case AUTH/3038/4/18, a Novartis employee had disseminated information referring to a prescription only medicine to contacts in his/her personal LinkedIn account and the company was found to be in breach of the Code including Clause 26.1. The Panel noted that a form of undertaking and assurance was an important document. Companies had to give an undertaking that the material in question and any similar material, if not already discontinued or no longer in use, would cease forthwith and give an assurance that all possible steps would be taken to avoid similar breaches of the Code in future (Paragraph 7.1 of the Constitution and Procedure). It was very important for the reputation of the industry that companies complied with undertakings. The Panel noted that both cases related to the alleged promotion of a prescription only medicine to the public via a social media channel, however, there were differences between the cases. The Panel noted, however, its ruling above of no breach of Clause 26.1 and thus ruled no breach of Clauses 29 and Clause 2 in relation to the allegation of a breach of undertaking in Case AUTH/3038/4/18.
Noting its comments above the Panel did not consider that the retweet constituted disguised promotion and ruled no breach of Clause 12.1.

The Panel noted that after reading the tweet, the complainant searched the internet for reference to the Novartis haematology masterclass and found the Association of Myeloid Neoplasms Practitioners (AMNP) website which contained a Novartis haematology academy flyer.

The Panel noted that the flyer at issue contained the Novartis logo and a website address for the haematology academy; it invited readers to register for future haematology events and access past meeting material. It also stated, 'Discover a growing collection of Novartis educational content and materials, easily accessible on one platform'. At the bottom of the flyer, it stated: 'Events are either organised or sponsored by Novartis Pharmaceuticals UK Ltd.' and 'This website [haematology academy] has been developed by Novartis Pharmaceuticals UK Ltd for use by HCPs [healthcare professionals] only and contains promotional material'. The Panel noted Novartis' submission that there was no active hyperlink to the haematology academy contained within the flyer and that if users typed in the URL address, or found it by an internet search, they would have to declare they were a health professional and register as the website was access restricted.

The Panel noted that the flyer at issue contained no direct or indirect reference to a specific medicine and therefore, in its view, did not require prescribing information. No breach of Clause 4.1 was ruled.

With regard to the allegation that the complainant was unclear of the relationship between Novartis and the AMNP, the Panel noted Novartis' submission that it had contributed to the establishment and the maintenance of the AMNP website by providing two grants.

The Panel noted that Clause 9.10 stated that material relating to medicines and their uses, whether promotional or not, and information relating to human health or diseases which is sponsored by a pharmaceutical company must clearly indicate that it has been sponsored by that company. The supplementary information to this clause stated, *inter alia*, that the declaration of sponsorship must be sufficiently prominent to ensure that readers of sponsored material were aware of it at the

outset. The wording of the declaration must be unambiguous so that readers would immediately understand the extent of the company's involvement and influence over the material. In the Panel's view, this was particularly important when companies were involved in the production of material circulated by an otherwise wholly independent party.

The Panel noted that the screen shot provided by the complainant referred to another named pharmaceutical company supporting the maintenance of the site. The Panel noted that Novartis had also provided financial support to AMNP for the maintenance and hosting of the website.

The Panel considered that the AMNP website declaration 'Developed with support from Novartis Pharmaceuticals UK Ltd' could have been clearer given Novartis was also providing support to AMNP for the website's ongoing maintenance; particularly as another company was listed as providing the support for the website maintenance. The AMNP website had a Novartis flyer for the haematology academy which Novartis submitted was uploaded following a decision by the AMNP steering group and without Novartis' involvement or influence. The Panel noted Novartis' submission that it did not have any influence over the AMNP, its website or the materials hosted upon it and it had no involvement in the flyer being made available on the AMNP website.

The Panel considered that, on balance, the declaration was not misleading as to the relationship between Novartis and the AMNP in relation to the website content where it appeared Novartis had no influence. The Panel therefore ruled no breach of Clause 9.10 based on the narrow allegation.

The Panel noted its comments above and did not consider that Novartis had failed to maintain high standards and ruled no breach of Clause 9.1.

**Complaint received** **27 February 2019**

**Case completed** **18 June 2019**

**CASE AUTH/3168/2/19**

# COMPLAINANT v JANSSEN

## Company website

**A contactable individual who described him/herself as a concerned UK health professional, complained about the Janssen Medical Cloud website. The website was described on its homepage as being for healthcare professionals providing information about Janssen, product information, medical education and resources for patient management by disease area. Links were included to prescribing information and the home page included that the website contained promotional content.**

**The complainant stated that Janssen Medical Cloud appeared to be a website that was promotional and had areas that probably should not be.**

**The complainant stated that he/she was initially concerned about the way medical was so overtly used on a promotional website but then he/she realised that this was merely the tip of the iceberg. The complainant highlighted a number of concerns.**

**The detailed response from Janssen is given below.**

**With regard to various allegations that changes to summaries of product characteristics (SPC) had not been reflected in prescribing information, the Panel ruled no breach of the Code. This applied to material about Edurant, Symtuza, Stelara and Zytiga. The Panel also ruled no breach in relation to Trevicta, Xeplion and Risperdal oral tablets and solution and Risperdal Consta in the Schizophrenia portfolio.**

**Breaches of the Code were ruled in relation to similar allegations about Trevicta, Xeplion and Risperdal Consta prescribing information within a presentation on Schizophrenia including that high standards had not been maintained.**

**The Panel ruled a breach of the Code as high standards had not been maintained in relation to an alleged failure to include all the special warnings and precautions for using Edurant. Warnings relating to pregnancy were not included in a table.**

**The failure to update references to when pages were last updated was not considered to be a matter covered by the requirements for prescribing information and no breach was ruled in relation to two similar allegations in this regard.**

**The Panel ruled no breach in that the use of a supressed zero in a graph did not exaggerate the differences between the products as alleged. A second graph which also used a suppressed zero was ruled in breach as in this instance the presentation exaggerated the differences between the products.**

**The Panel ruled a breach as it considered a reference to 'the safe and effective use of Janssen medicines' in a 'meet the team' section might be seen as a claim that such medicines were safe.**
**The Panel ruled breaches of the Code as a Tremfya video did not have the up-to-date prescribing information. A further breach was ruled due to the lack of clear prominent statement as to where the prescribing information could be found.**

**No breach was ruled with regard to certification of presentations published in the oncology section on the website.**

**The Panel ruled that the facility for a health professional to forward materials to colleagues did not amount to disguised promotion. It would be clear to recipients that Janssen had created the email template and that the content was from the company. Prescribing information was available on the website accessed by the link and the email creation was certified as part of the website. No breaches of the Code were ruled.**

**The Panel did not consider that the website was disguised promotion. It was clearly promotional. The Panel ruled no breach in this regard.**

**The Panel did not consider that the complainant had shown on the balance of probabilities that the training of Janssen staff failed to meet the requirements of the Code and ruled no breach of the Code.**

**The Panel considered it was very important that prescribing information was up-to-date. It noted that there were some errors on the website and also noted its rulings above. The Panel considered therefore that high standards had not been maintained and ruled a breach.**

**The Panel noted the complainant stated that if the majority of the allegations were found to be true, then he/she was alleging a breach of Clause 2. The majority of allegations had not been ruled in breach. The Panel noted the errors with out of date prescribing information and its ruling that high standards had not been maintained. It also noted Janssens's submission that the up to date prescribing information was available on the home page. Clause 2 of the Code was a sign of particular censure and reserved for such use. The Panel considered that based on the allegations, on balance, the circumstances did not warrant a ruling of a breach of Clause 2 of the Code.**

A contactable individual who described him/herself as a concerned UK health professional, complained about the Janssen Medical Cloud website. The website was described on its homepage as being for healthcare professionals. It provided information about Janssen and gave access to product information, medical education and resources

for patient management by disease area. Links were included to prescribing information and the home page included that the website contained promotional content.

**COMPLAINT**

The complainant stated that Janssen Medical Cloud appeared to be a website that was promotional and had areas that probably should not be. The website was clearly promotional – the landing page stated 'This website contains promotional content'. The complainant stated that he/she was initially concerned about the way medical was so overtly used on a promotional website but then he/she realised that this was merely the tip of the iceberg.

The complainant highlighted the following:

**1 Edurant (rilpivirine) (an antiretroviral for treatment of HIV)**

The complainant referred to a table of special warnings which presented material from the summary of product characteristics (SPC) 2016. The complainant stated that the SPC had been updated several times since then, including to both special warnings and pregnancy and lactation. Although the page had apparently been updated in 2017, the references had been last accessed in 2016 so were out-of-date when the website was last updated.

The prescribing information was also alleged to be out-of-date as the version was dated 2017. The complainant alleged a breach of Clause 4.1.

At the bottom of the webpage there was a button which stated 'recommend this content to a colleague'. Pressing this created an email that health professionals could send to their colleagues on behalf of Janssen. This used health professionals to contact their colleagues. This was true of many of the pages of the website. The complainant alleged breaches of Clauses 4.1, 4.2, 4.3, 4.4, 12.1 and 14.1.

**2 Prezista (darunavir) (an antiretroviral for the treatment of HIV)**

The complainant stated that a graph demonstrated improved renal function after switching from alternative treatments. Whilst there was a difference, the estimated glomerular filtration rate (eGFR) on the y axis only went from 60 to 105, which exaggerated the difference between the two categories. The complainant alleged a breach of Clause 7.2.

There was also the same issue on the graph below; discontinuation rates for treatment-experienced patients ended at 0.2 as opposed to 0 which the complainant alleged exaggerated the difference between the treatments in breach of Clause 7.2.

Again, there was a button that stated 'recommend this content to a colleague'. This created an email that health professionals could send to their colleagues on behalf of Janssen.

**3 Symtuza (darunavir, cobicistat, emtricitabine, tenofovir) (a fixed combination of antivirals for treating HIV)**

The complainant alleged that the Symtuza prescribing information was out-of-date, in breach of Clause 4.1.

Again, at the bottom of the webpage there was a button that stated 'recommend this content to a colleague'. This created an email that health professionals could send to their colleagues on behalf of Janssen.

**4 Schizophrenia section**

The complainant alleged that the prescribing information for Trevicta, Xeplion, Invega (all various pharmaceutical forms of palperidone), Risperdal and Consta (different pharmaceutical forms of risperidone) were all out-of-date, in breach of Clause 4.1.

The references of the page had not been reviewed after the significant updates.

**5 Pharmacy Academy – Schizophrenia**

The complainant stated that with regard to the Pharmacy Academy 2017, most of the links did not work. The link which worked included three lots of prescribing information at the end of the slides. The complainant alleged the prescribing information was out-of-date in breach of Clause 4.1.

**6 Rheumatology Section - Stelara**

The complainant alleged that in the Rheumatology section of the website, the prescribing information for Stelara (ustekinumab) was out-of-date; in breach of Clause 4.1.

**7 'Meet' the medical team**

The complainant noted that via a link to medical education readers could 'meet' the medical team. In each instance, there was a biography of what the team members could do for health professionals. Included in every profile was the statement 'Address your questions concerning the safe and effective use of Janssen medicines based on available data'. As this wording was identical in all the profiles throughout the website it appeared to be the company boilerplate. With each use the complainant alleged a breach of Clause 7.9.

**8 Tremfya (guselkumab) Video – medical education**

The complainant alleged that no prescribing information was available for the Tremfya (guselkumab) video. The complainant alleged a breach of Clauses 4.1 and 4.6.

**9 Oncology Section**

The complainant alleged that in the oncology section, there were fifteen slide decks all of which described how they would be altered before

they were finally used. The complainant alleged a breach of Clause 14.1 in each instance. None of the slide decks had prescribing information attached, but it was, nonetheless, available by following a link. The prescribing information was, however, out-of-date and a breach of Clause 4.1 was alleged.

**10 General**

The complainant submitted that there might be other issues on the website, but he/she did not have the time to investigate more deeply.

In conclusion, the complainant alleged that the Janssen website was dangerously out-of-date and, if relied on by health professionals, could lead to unsafe clinical prescribing decisions. It also appeared designed to blur what the sales department and the medical department did.

The magnitude of the errors, both in number and in severity, made the complainant wonder how this could have not been picked up by any person over the years – training appeared to be inadequate in breach of Clause 16.1.

Given that historically a finding of a breach of Clause 9.1 had been given for one out-of-date prescribing information, this should be viewed in each instance.

If the majority of the allegations were found to be true, the complainant alleged a breach of Clause 2.

**RESPONSE**

Janssen explained that the Medical Cloud website was a web-based platform that served as a single repository for product and therapy area content directed at medical professionals. The name of the website identified the target audience and separated it from any other Janssen sites eg corporate or patient etc. The website was certified in accordance with Clause 14.1.

Janssen noted that the complainant had correctly highlighted the fact that the website contained promotional content. There was no attempt to disguise the fact that the website included promotional content. This was intended to be a promotional website and all content was presented in that context.

In addition, the website contained broader information that might be of interest to health professionals, including educational resources, tools for health professionals to use with patients, medical information contact details and adverse event reporting information. All content about Janssen medicines, be that branded/promotional or non-branded/educational, was in accordance with the relevant marketing authorization and licensed indications.

Janssen asserted that there was no attempt to disguise promotional content and therefore it denied a breach of Clause 12.1. Nevertheless, Janssen had made the disclaimer more prominent by incorporating it into the title and main image of the homepage.

With regard to the prescribing information, Janssen acknowledged a breach in relation to two items, a downloadable presentation and a video clip (see Points 5 and 8 below).

On the homepage, there was a link to a web-based repository of the most up-to-date prescribing information for each of the marketed products. When an SPC change necessitated a change to the prescribing information, the regulatory team (in consultation with medical affairs) implemented and communicated the changes in line with Janssen's processes. In addition, the regulatory team also approved the web version of the prescribing information to ensure that it had been correctly transposed and formatted, before being posted on the prescribing information portal.

Prescribing information could be accessed from the home page for all promoted products. In addition, each promotional webpage had links to the appropriate prescribing information for therapy area specific medicines.

Thus, Janssen submitted that health professionals had clear access to the most up-to-date prescribing information on the website.

**1 Edurant**

Janssen stated that the prescribing information for Edurant was last updated in August 2017. Since then, there had been the following two updates to the SPC:

a) October 2018 – Section 4.4: To add warning 'autoimmune hepatitis' within parenthesis to 'Autoimmune disorders'
b) January 2019 – Section 4.9: Overdose - removal of activated charcoal to manage overdose.

Janssen submitted that neither of the above SPC changes mandated changes to the prescribing information, therefore, the prescribing information for Edurant was up-to-date and not in breach of Clause 4.1.

Janssen submitted that the relevant section of the website was last reviewed on 10 October 2017, the last revision of the SPC was 24 August 2018. The updates since July 2016 (the stated access date in the references) to the SPC included:

- Removal of black triangle – not relevant to the table
- Drug-drug interaction (DDI) with simeprevir – No dose adjustment required and therefore not relevant to the table
- 'autoimmune hepatitis' within parenthesis to 'autoimmune disorders' – not relevant to table
- Overdose -removal of activated charcoal to manage overdose – not relevant to table
- Inclusion of additional pregnancy data – additional information added about pharmacokinetic data.

Janssen submitted that as the SPC amendments above were not relevant to the table, it was not considered necessary to update the table. Whilst Janssen accepted that the date of last access (July 2016) was not updated to reflect the review date in 2017, the link directed the user to the most recent SPC on the eMC. Upon reflection, Janssen noted that the original table should have included information on pregnancy as commented on by the complainant. As such, Janssen had since removed the infectious disease sections of the website pending further revision.

The response to the recommend content to a colleague allegation was covered in point 10 below.

**2 Prezista**

Janssen submitted that the graph, which demonstrated improved renal function, had been faithfully reproduced from the publication. A lower eGFR limit of 60ml/min/1.73m$^2$ was consistent with the internationally accepted cut off above which kidney function was considered normal. The message was not misleading insofar as the gradual decline in eGFR was reversed/stabilised with a switch from either ATV/r to DRV/r or LPV/r to DRV/r. Janssen denied a breach of Clause 7.2.

Whilst Janssen accepted that the second graph of discontinuation rates for treatment-experienced patients started at 0.2, it did not represent a distorted impression of the data given that 80% of the range was included. Starting the Y-axis at zero would not alter the marked and statistically significant difference between LPV and DRV nor would it reduce the statistically significant difference seen between DRV and the other agents. Janssen denied a breach of Clause 7.2.

Nevertheless, Janssen would review the graphs pending further revision of the infectious disease section of the website.

**3 Symtuza**

Janssen submitted that the prescribing information for Symtuza was last updated in November 2018, at the same time as the most recent SPC (November 2018). The link on the website was to the Symtuza prescribing information dated November 2018. Janssen denied a breach of Clause 4.1.

**4 Schizophrenia portfolio**

Janssen provided a table which included the relevant process dates for SPC and prescribing information updates for Trevicta, Xeplion, Invega, Risperdal tablets and oral solution and Risperdal Consta. The date of last revision of the prescribing information reflected the 'date of revision of the text' specified in Section 10 of the SPC and not the date the SPC was 'Last updated on the Electronic Medicines Compendium (eMC)'. Janssen submitted that the prescribing information for all the medicines referred to were current. Janssen denied a breach of Clause 4.1.

Janssen pointed out that whilst the complainant had not identified specific references of concern, it was assumed that the complaint related to the following references due to there being specific mentions of the date of last access:

1 Xeplion. Summary of Product Characteristics. 2018. [Last accessed: May 2018].
2 Trevicta. Summary of Product Characteristics. 2018. [Last accessed: May 2018].

The table below detailed the claims made on the webpage as they related to the latest SPC. Since May 2018 none of the changes to the SPC affected the substantiation of the respective claims. Janssen submitted that the changes in the September SPC did not include any revisions to the section to which the claims were referenced. As such the claim was substantiated by the reference and was not in breach of the Code.

| Claim | Source of substantiation from latest SPC |
|---|---|
| **Previous treatment (oral risperidone or paliperidone)1** | **4.2 Therapeutic indications:** Xeplion is indicated for maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone. |
| **4 per year dosing with Trevicta2** | **4.2 Posology and method of administration** Following the initial TREVICTA dose, TREVICTA should be administered by intramuscular injection once every 3 months (± 2 weeks). |

Janssen acknowledged that the text should have been updated to indicate that the references had been checked more recently (in October 2018) but this was not part of the complaint *per se* and did not impact the accuracy of the reference itself.

**5 Schizophrenia slides – Pharmacy academy**

Janssen noted that this complaint related to a downloadable presentation on schizophrenia. This presentation was available from the URL provided by the complainant from the Big Questions Meeting webpage, which contained prominent links to the correct and current prescribing information for all products at the top.

However, Janssen acknowledged that there had been a breach of Clause 4.1 relating to the prescribing information contained within the presentation. The prescribing information for each of the 3 products mentioned Trevicta, Xeplion and Risperdal Consta attached to the actual downloadable presentation should have been amended in line with SPC updates in September 2018 in relation to Sections 4.4 and 4.5 – Caution is warranted in patients receiving both psychostimulants (eg, methylphenidate) and paliperidone concomitantly, as extrapyramidal symptoms could emerge when adjusting one or

both medications. Gradual withdrawal of stimulant treatment is recommended. Janssen accepted a failure to maintain high standards in breach of Clause 9.1.

All prescribing information containing materials submitted for copy approval were required by the Janssen SOP to be marked as 'containing PI' in the relevant job bag information field. This facilitated identification of materials that required withdrawal/ revision at the time of a prescribing information update. Investigation of the underlying cause for failing to withdrawal this presentation had identified an individual error which resulted in this item not being flagged in the company's approval system as containing prescribing information. Consequently, it was missed in the recall process when the SPC and prescribing information were updated in September 2018. This presentation was withdrawn on 12 March 2019. In line with Janssen's ongoing compliance training framework, Janssen committed to using this case to emphasise the importance of correctly logging all materials containing prescribing information.

**6 Rheumatology section - Stelara**

Janssen submitted that the prescribing information for Stelara was last updated in April 2018. Since then, there had been the following two revisions to the SPC text:

1 July 2018
- Section 4.4: addition on information on sodium content
- Section 4.8: deletion of immunogenicity paragraph
- Section 5.1: addition on immunogenicity paragraph.

2 November 2018
- Section 4.4: addition of paragraph on respiratory hypersensitivity reactions.
- Section 4.8: addition of allergic alveolitis and eosinophilic pneumonia under frequency of rare.

Janssen submitted that neither of the above revisions to the SPCs mandated updates to the prescribing information, therefore, the prescribing information for Stelara on the website in question was up-to-date and not in breach of Clause 4.1.

**7 Meet the team link to medical colleagues**

Janssen stated that as described previously, content under each therapy area was signposted as being of promotional, medical educational or other utility. The links to the medical team were only available from the medical education content pages, in the case of rheumatology, from the Janssen eXchange Hub.

Each of the team members had a short description of their individual experience, what their MSL role could offer the health professional, their qualifications and any publications.

Regarding the allegation of a breach of Clause 7.9, Janssen did not agree that the description of the service the MSL could offer implied either directly or indirectly that any Janssen medicines were 'safe'. Janssen denied a breach of Clause 7.9.

**8 Tremfya video**

The prescribing information for Tremfya could be found at the end of the video and therefore the video complied with the requirements of Clause 4.5 and did not breach Clause 4.6. Janssen accepted that the prescribing information was out-of-date and was therefore in breach of Clause 4.1. This video had been withdrawn as of 22 March 2019.

**9 Oncology slides**

Janssen stated that there were 15 presentations in the Medical Education, Prostate Cancer Hub section under the 'slides and case studies' tab. On clicking this tab, the health professional was presented with a selection of presentations for viewing and download. All the presentations related to disease area topics of interest, with a small number discussing medicines in a balanced manner. In line with the Code, prescribing information was clearly available and accessible from the top of the same website page.

The prescribing information for Zytiga (February 2019) was current with the most recent revision of the SPC text which took place on 26 February 2019. Janssen denied all breaches of Clause 4.1 in relation to these presentations.

Janssen accepted that all 15 presentations had an in-house comment on the standard disclaimer slide, which should have been removed before final certification. Nevertheless, each of the presentations had been certified with the comment in place and published on the website as approved in final form, with the comment in situ and in line with the requirements of Clause 14.1.

The comment referred to by the complainant was:

> 'Reviewers please note – disclaimer slide included for review purposes in all speaker presentations but will be included only once when the showreel is compiled for the Summit meeting – ok?'

There was no instruction for content slides to be altered, and signatories certified the slides with this information to hand. Janssen denied a breach of Clause 14.1

**10 Recommend content to a colleague**

Janssen stated that it was not clear from the complainant as to why he/she considered the clauses cited had been breached.

The 'recommend to a colleague' functionality was available at the bottom of some website pages. Upon clicking it, an outlook email from the referring health professional was opened bearing the following:

'Subject: *Recommended content from Janssen.*

Content: *I thought this content from Janssen would interest you. Link to JMC page.'*

The reference to Janssen in the header and in the opening sentence was a clear indication that the content was not independent. Since there was also nothing in the text to indicate the material was non-promotional, it was difficult to see how any recipient of the email could be tricked into opening it. Consequently, Janssen denied any allegation of Clause 12.1.

The email generated did not contain any product information (other than in some cases the product name within the link). Janssen did not believe that in this context there was a requirement for prescribing information to be included in the email and therefore it refuted any breaches of Clauses 4.1, 4.2, and 4.4. Furthermore, the only reference to a brand might be found in the details of the web link. As such, Janssen did not agree that the non-proprietary name was required and therefore denied a breach of Clause 4.3.

The email's creation was certified as part of the website itself. No further certification was necessary; consequently, the requirements of Clause 14.1 had already been met.

**11 General**

Janssen stated that all personnel involved in the creation and approval of content were appropriately trained on the requirements of the Code. This included online modules, SOP training, mentoring, supervision and Code updates delivered every 3 months by a third-party compliance agency. Janssen denied a breach of Clause 16.1.

Given the scale of the website, approval of content was done in sections or pages depending on the interconnectivity. Individual pieces for upload onto the website were approved as standalone items which sat in a separately approved frame. This facilitated the dynamic nature of web-based content whilst reducing the need to approve the entire site each time a change was made. This meant that there was no specific date on which the entire website was approved. All web-based content was on the current materials list and it was Janssen's policy to review and reapprove all web-based content at least every 12 months. All content that was flagged in the approval system as containing prescribing information was updated when the supporting prescribing information changed. Investigation had confirmed that the 2 items that were not updated following a prescribing information change were as a result of individual error. As indicated previously, Janssen would emphasise to originators and signatories the importance of checking that materials were correctly flagged as containing prescribing information or not.

Finally, as most of the items were properly clarified, Janssen denied a breach of Clause 2.

**PANEL RULING**

The Panel addressed the specific points raised by the complainant as follows.

**1 Edurant**

The Panel noted the material provided by Janssen was a webpage headed 'Edurant' and included sections on tolerability, efficacy and DDIs (drug-drug interactions) which included a table headed 'Special warnings and precautions when prescribing Edurant' referenced to the Edurant SPC 2016. The Panel noted Janssen's submission that the information was reviewed on 10 October 2017 and the last revision of the SPC was 24 August 2018. The company did not amend the table as in its view the amendments to the SPC since July 2016 were not relevant to the table. However, the date of last access (July 2016) was not updated.

It was not entirely clear whether the table headed 'Special warnings and precautions when prescribing Edurant' was part of the section 'drug-drug interactions'. The Panel noted that the table included more than simply information about drug-drug interactions but did not include any of the special warnings and precautions for use in Section 4.4 of the Edurant SPC including information on pregnancy.

Section 4.6 of the July 2017 SPC Fertility, pregnancy and lactation stated that there was no or limited data from the use in pregnant women and that animal studies did not indicate direct or indirect harmful effects with respect to reproductive toxicity. It also stated that as a precautionary measure it was preferable to avoid the use of Edurant during pregnancy. The August 2017 SPC had an update to Section 4.6 to include the additional information that lower exposures of Edurant were observed during pregnancy, therefore viral load should be monitored closely. In addition, information was added to Section 4.4 Special warnings and precautions for use which stated, *inter alia*, that Edurant should be used during pregnancy only if the potential benefit justified the potential risk.

The Panel considered that although the table appeared under a section headed drug-drug interactions (DDIs), given the subheading to the table 'Special warnings and precautions ...' and its content, the table would be seen as including all the relevant information. The special warnings and precautions for use from Section 4.4 of the Edurant SPC, including pregnancy, should have therefore been included in the table and the failure to do so was misleading and high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel considered that the references were not up-to-date but this was not a matter covered by Clause 4.1 as alleged by the complainant; Clause 4.1 related to the provision of prescribing information. No breach of Clause 4.1 was ruled in that regard.

With regard to the allegation that the prescribing information was out-of-date, the Panel noted Janssen's submission that it was last updated in August 2017 and that the two SPC updates since this date did not mandate changes to the prescribing information. The complainant bore the burden of proof and, in the Panel's view, he/she had

not established that the prescribing information was not up-to-date. The Panel thus ruled no breach of Clause 4.1.

The allegation regarding recommend content to a colleague was covered in point 10 below.

**2 Prezista**

The Panel noted that the graph compared the effects of atazanavir or lopinavir on eGFR decline prior to a switch to darunavir (all in addition to ritonavir) and the effect of that switch on eGFR. Although the y axis started at 60, the Panel did not consider that this necessarily meant that the graph was misleading. The graph on the Janssen website was similar to that in the published paper. The data presented did not go below 90 so the space between 60 and 90 was blank. The values for mean (95% confidence interval) eGFR slope estimates pre and post-switch were given. All the data was presented, there were no values which were off the scale. In the circumstances the Panel did not consider that the presentation exaggerated the differences between the products as alleged and therefore ruled no breach of Clause 7.2.

The second graph referred to by the complainant was headed 'Discontinuation rates for treatment-experienced patients'. Real world data for rilpivirine, darunavir, raltegravir, efavirenz, atazanavir, entecavir and lopinavir were presented with the y axis scale (proportion of patients on treatment) starting at 0.2 and finishing at 1. The graph was positioned under a subheading 'the majority of treatment-experienced patients continue with their treatment when on darunavir'. The Panel considered that this graph was misleading as it gave the impression due to the absence of some of the y axis (0.2-0) that most, if not all, patients on lopinavir discontinued therapy and this was not so.

The Panel considered that the presentation exaggerated the differences between the products as alleged and ruled a breach of Clause 7.2 of the Code.

The allegation regarding recommend content to a colleague is covered in point 10 below.

**3 Symtuza**

The Panel noted the submission from Janssen that the prescribing information for Symtuza was last updated in November 2018 which was the same date as the most recent SPC and the prescribing information links on the homepage and each promotional webpage were to the up-to-date information. The Panel thus ruled no breach of Clause 4.1.

The allegation regarding recommend content to a colleague is covered in point 10 below.

**4 Schizophrenia**

The Panel noted the submission from Janssen that the prescribing information links on the homepage and each promotional webpage were to the up-to-date information. The Panel thus ruled no breach of Clause 4.1 for each of the products.
The Panel noted Janssen's submission that the complainant had not provided specific concerns regarding the references. Janssen provided further information. The company acknowledged that the references should have been updated to indicate that they had been checked more recently. The company submitted that this was not part of the complaint and did not impact the accuracy of the reference itself.

The Panel considered that the references were not up-to-date but this was not a matter covered by Clause 4.1 as alleged by the complainant; Clause 4.1 related to the provision of prescribing information. No breach of Clause 4.1 was ruled in that regard.

**5 Pharmacy Academy**

The Panel noted from Janssen's submission that the prescribing information for Trevicta, Xeplion and Risperdal Consta within the presentation had not been updated to reflect SPC updates in relation to Sections 4.4 and 4.5 and the need for caution in certain patients. A breach of Clause 4.1 was ruled for each out-of-date prescribing information. The Panel ruled that Janssen had failed to maintain high standards in breach of Clause 9.1 as acknowledged by the company.

6 Rheumatology Section – Stelara

The Panel noted the submission from Janssen that the prescribing information links on the homepage and each promotional webpage were to the up-to-date information. The Panel noted Janssen's submission that the Stelara prescribing information was last updated in April 2018 and since that date there had been two revisions to the SPC which Janssen stated did not mandate updates to the prescribing information. The complainant bore the burden of proof and, in the Panel's view, he/she had not established that the prescribing information was not up-to-date. The Panel thus ruled no breach of Clause 4.1 in relation to Stelara.

**7 Meet the medical team**

The Panel noted Janssen's submission that the links to the medical team were only available from the medical education content pages. The Panel queried whether readers would see the site as containing promotional and non-promotional elements. The Panel noted that the Janssen exchange hub referred to events, including videos, one of which referred to an overview of a Janssen product (guselkumab) others referred to treating conditions in which Janssen had an interest.

The website included an option to meet the team, providing contacts for MSLs and the medical education manager. The further details about one of the MSLs included a list of what an MSL could do for you and the first point was 'address your questions concerning the safe and effective use of Janssen medicines based on available data'. This appeared to be a standard description as it was included in the profiles of all the MSLs named.

The Panel considered that the reference to the safe and effective use of Janssen medicines might be seen as a claim that such medicines were safe. Although there might be a difference between the medicine being safe and the safe use of that medicine Clause 7.9 stated that the word 'safe' must not be used without qualification. Clause 7 was not limited to promotional material. The Panel considered that on balance the reference to safe and effective use of Janssen's medicines did not meet the requirements of Clause 7.9 and a breach was ruled.

**8 Tremfya video**

The Panel noted Janssen's submission that prescribing information was provided at the end of the video but it was not up to date. In that regard the Panel ruled a breach of Clause 4.1 of the Code as acknowledged by Janssen. The Panel noted that it appeared from the information provided by Janssen that the video was no longer available and the webpage on which the video had appeared did not contain a clear prominent statement as to where the prescribing information could be found. Similarly the beginning of the video did not include such a statement. The Panel therefore ruled a breach of Clause 4.6.

**9 Oncology section**

The Panel noted the submission from Janssen that the prescribing information was clearly available and accessible from the webpage and that the prescribing information for Zytiga was up-to-date. The Panel thus ruled no breach of Clause 4.1.

With regard to the internal comment for reviewers which had been published, the Panel noted Janssen's submission that the presentations had been certified with the comment in place. The Panel considered that what was published on the website had been certified as required by the Code and thus ruled no breach of Clause 14.1 of the Code.

**10 Recommend content to a colleague**

With regard to the facility for health professionals to forward materials to colleagues (allegations in points 1, 2, and 3 of the complaint), the Panel noted Janssen's submission that the email generated when using this facility referred to Janssen in the subject and in the content.

The Panel considered that it would be sufficiently clear to recipients of these emails that Janssen had created the email template for one health professional to send to another and that the content was from the Janssen website.

The Panel noted that promotional material did not need to be labelled as such, however, it must not be disguised, and the identity of the responsible pharmaceutical company or a pharmaceutical company's involvement must be obvious at the outset. In the Panel's view, those receiving the emails from health professionals would be aware that the material was from Janssen, the example provided included a product name in the URL, and would be likely to assume it was promotional. Further the complainant had not proved on the balance of probabilities that the material accessed from the emails in question constituted disguised promotion. The Panel ruled no breach of Clause 12.1.

The content of the email was a link to the Janssen material. The example provided by Janssen included a URL link that mentioned a product name but with no further information about the product in the email. The Panel noted Janssen's submission that prescribing information was on the webpage accessed from the URL. In these circumstances, the Panel ruled no breach of Clauses 4.1, 4.2, 4.3 and 4.4.

Janssen submitted that the email creation was certified as part of the website. Each individual email was not certified. The Panel noted that the differences between the emails would be the address of the sender and of the recipient health professional and any other content added by that health professional. The Panel considered that in the circumstances the certification requirements had been met. No breach of Clause 14.1 was ruled.

**11 General**

The Panel noted Janssen's submission that the website had been certified in accordance with Clause 14.1 ie as promotional material. The Panel did not consider that the website was disguised promotion. It was clearly promotional. The Panel ruled no breach of Clause 12.1.

The Panel did not consider that the complainant had shown on the balance of probabilities that the training of Janssen staff failed to meet the requirements of Clause 16.1. The Panel noted the company's submission about the training it provided staff. The Panel ruled no breach of Clause 16.1.

The Panel considered it was very important that prescribing information was up-to-date. It noted that there were some errors on the website and also noted its rulings above. The Panel considered therefore that high standards had not been maintained and ruled a breach of Clause 9.1.

The Panel noted the complainant's allegation was that if the majority of the allegations were found to be true then he/she was alleging a breach of Clause 2. The majority of allegations had not been ruled in breach. The Panel noted the errors with out of date prescribing information and its ruling of a breach of Clause 9.1 and Janssens's submission that the up to date prescribing information was available on the home page. Clause 2 of the Code was a sign of particular censure and reserved for such use. The Panel considered that based on the allegations, on balance, the circumstances did not warrant a ruling of a breach of Clause 2 of the Code.

**Complaint received** **27 February 2019**

**Case completed** **27 June 2019**

**CASE AUTH/3169/3/19**

# VOLUNTARY ADMISSION FROM OTSUKA EUROPE

## Revision of Jinarc SPC

**Otsuka Pharmaceuticals Europe, voluntarily admitted that it might have breached the Code with regard to updates to the Jinarc (tolvaptan) summary of product characteristics (SPC). Jinarc was used in certain patients with chronic kidney disease.**

**As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Otsuka Europe.**

**Otsuka Europe explained that there had been two parallel revisions to the Jinarc SPC since November and these had been communicated to the marketing authorization holder and all relevant European affiliates. The preliminary investigation concluded that communication to the affiliates on 14 February could have been clearer on this point.**

**Otsuka Europe regretted that communications to EU affiliates about SPC revisions had caused confusion and that as a result there was a Jinarc SPC available on the eMC from 15 February to 1 March which contained the latest revision (addition of gout) but not the preceding revision (addition of blister wallet cards). Otsuka Europe was concerned that there might have been a breach of the undertakings given in Cases AUTH/3041/6/18 and AUTH/3123/11/18.**

**Otsuka Europe stated that it also became aware in January 2019 that there was a mistake in the packaging and release of the Jinarc package leaflet in that the previous version of the package leaflet was packaged with the product. The company notified the EMA and the Medicines and Healthcare products Regulatory Agency (MHRA) on 17 January 2019 about that situation. During the following days the issue was discussed with the EMA. The EMA confirmed on 6 February that no Direct Healthcare Professional Communication (DHPC) was required.**

**The detailed response from Otsuka Europe is given below.**

**The Panel noted that there had been two parallel revisions to the Jinarc SPC (addition of blister in wallets cards with new marketing authorization numbers and addition of gout as a common adverse drug reaction) and that the two revisions were each subject to separate applications to the EMA and therefore a combined consolidated version also had to be approved by the EMA.**

**The Panel noted, based on Otsuka Europe's submission, that when two or more variation applications were submitted and/or assessed in parallel by the EMA, the procedures were kept separate, and further noted Otsuka Europe's submission that, in this case, having an SPC with gout but without the preceding blister wallet cards revision was unavoidable. However, the Panel noted Otsuka Europe's submission that the communication to the affiliates dated 14 February regarding this matter could have been clearer so they could have planned how to deal with this situation, and that the communication regarding the consolidated SPC sent to the affiliates on 26 February had not followed the relevant SOP and caused confusion in the affiliates.**

**The Panel considered that the lack of clear communication by Otsuka Europe to its affiliates, which was compounded by the failure to follow, and lack of consistent application of, the relevant SOP, meant that Otsuka Europe had failed to maintain high standards and a breach was ruled.**

**The Panel noted that in Case AUTH/3041/6/18, Otsuka Europe was found in breach of the Code for promotional materials either missing prescribing information or not containing the latest version of the prescribing information, for Otsuka Europe's governance of materials falling below acceptable standards, and Clause 2 for, *inter alia*, not providing prompt communication to Otsuka UK regarding SPC updates and poor governance which the Panel had considered had potential safety implications. Although there was some overlap between Case AUTH/3041/6/18 and the current case, the Panel noted that there were important differences. The subject matter of the former did not include the accuracy of communications about SPC updates in relation to Jinarc. The voluntary admission in Case AUTH/3169/3/19 did not refer to use of materials with the incorrect prescribing information. The Panel therefore considered, on balance, that the subject matter of the current case was sufficiently different to Case AUTH/3041/6/18 such that there was no breach of the undertaking given in that case. The Panel therefore ruled no breach of the Code including Clause 2 in this regard.**

**In relation to the admission of a breach of undertaking and Case AUTH/3123/11/18, Otsuka Europe referred to the email from Global Regulatory Affairs Region Europe dated 26 February 2019 and failure to follow process and causing confusion. In Case AUTH/3123/11/18, Otsuka Europe was found in breach of, *inter alia*, Clause 9.1 for lack of clear and consistent instructions to employees and third parties in relation to SPC changes and Clause 2 for its failure to timely and robustly address inadequacies in this process. The Panel considered that the breach of Clause 9.1 for the lack of clear communication to its affiliates and lack of consistent application of the relevant SOP in the current case (Case AUTH/3169/3/19) meant that Otsuka Europe had breached the undertaking given in Case AUTH/3123/11/18. The Panel therefore ruled a breach of Clause 29. The Panel considered that Otsuka Europe's breach of undertaking meant that it**

**had brought discredit upon, and reduced confidence in, the pharmaceutical industry and a breach of Clause 2 was ruled.**

**The Panel noted Otsuka Europe's admission in relation to an out-of-date package leaflet being packaged with Jinarc at the manufacturing site. The Panel noted Otsuka Europe's submission that the manufacturing site was notified on 12 October 2018 of an upcoming revision to the leaflet with an implementation of 30 November 2018 but it mistakenly used the previous version. The Panel considered that Otsuka Europe had been let down by its manufacturing site. The Panel considered that the package leaflet was an important document for patients and such an error meant that Otsuka Europe had failed to maintain high standards and a breach of the Code was ruled. The Panel considered that a breach of Clause 2 was a sign of particular censure. The Panel noted that Otsuka Europe had liaised with the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) with regard to this error and noted the actions Otsuka Europe submitted that it had agreed with the EMA on the matter. The Panel considered that, in these particular circumstances, and on balance, no breach of Clause 2 was warranted.**

Otsuka Pharmaceuticals Europe Ltd, voluntarily admitted that it might have breached the Code with regard to updates to the Jinarc (tolvaptan) summary of product characteristics (SPC). Jinarc was used in certain patients with chronic kidney disease.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Otsuka Europe.

**VOLUNTARY ADMISSION**

Otsuka Europe considered that there might have been a breach of the Code in relation to recent updates to the Jinarc SPC. Otsuka Europe explained that there had been two parallel revisions to the Jinarc SPC since November and these had been communicated to the marketing authorization holder and all relevant European affiliates. They were:

- addition of blister in wallets cards with new marketing authorization numbers – communicated to EU affiliates by Otsuka Europe medical affairs and Otsuka Global Regulatory Affairs Region Europe on 21 December 2018, then with a corrected prescribing information on 10 January 2019 (Case AUTH/3151/1/19 contained details of this issue)
- addition of gout as a common side-effect – communicated as before by Otsuka Europe and Otsuka Global Regulatory Affairs Region Europe to affiliates on 14 February 2019.

In both cases, as well as attaching the revised prescribing information, a word version of the SPC was attached to the notification email to the affiliates, and in the case of Otsuka UK, the word version of the SPC was provided to the electronic Medicines Compendium (eMC) so that the revised SPC could be uploaded. In relation to the marketing authorization holder and wallet blister card revision, Otsuka UK updated the eMC on 4 January 2019 and in relation to the addition of gout, it updated the eMC on 15 February 2019.

On 26 February there was a further copy of the Jinarc SPC emailed by Global Regulatory Affairs Region Europe without Otsuka Europe medical affairs inclusion which stated:

> 'We have now received a confirmation from EMA [European Medicines Agency] to use the consolidated SmPC [summary of product characteristics], including all previous changes in clean version. This will also be published at EMA website (EPAR) [European Public Assessment Report] soon.
>
> Attached you can find the recent consolidated Jinarc approved SmPC (in all languages – clean version) for your implementation where required.'

There were no other attachments to the email other than the SPC.

Otsuka UK queried the email given that the SPC circulated on 14 February had already been implemented, and received the response:

> 'Please replace with new SPC from 25 Feb sent to you today.
> Clarification:
> Two procedures of Jinarc were ongoing in parallel (Wallet and Gout). EMA has approved both SmPCs separately.
> The SmPC from 14 Feb does not includes [sic] last variation of Wallet.'

A preliminary investigation into this by Otsuka Europe medical affairs and Global Regulatory Affairs Region Europe had clarified that the two revisions to the Jinarc SPC were each subject to separate applications to the EMA thus a combined consolidated version had to be approved by the EMA:

- addition of blister in wallets cards
- addition of gout as a common adverse event
- the consolidated SPC of the above mentioned applications (wallet cards and gout).

All three SPCs were approved separately by the EMA and communicated to affiliates according to when the approval was communicated to Global Regulatory Affairs Region Europe. The preliminary investigation concluded that communication to the affiliates on 14 February could have been clearer on this point.

Otsuka Europe regretted that communications to EU affiliates about SPC revisions had caused confusion and that as a result of the actions noted above, there was a Jinarc SPC available on the eMC from 15 February to 1 March (when the consolidated SPC was uploaded following receipt by Otsuka Europe of the word version on 27 February) which contained the latest revision (addition of gout) but not the preceding revision (addition of blister wallet cards). Otsuka Europe was concerned that there might have

been a breach of the undertakings given in Cases AUTH/3041/6/18 and AUTH/3123/11/18, contrary to the requirements of Clauses 9.1 and 2.

Otsuka Europe stated that it also became aware in January 2019 that there was a mistake in the packaging and release of the Jinarc package leaflet at the manufacturing site in the UK, in that the previous version of the package leaflet was packaged with the product. The company notified the EMA and the Medicines and Healthcare products Regulatory Agency (MHRA) on 17 January 2019 about that situation. During the following days the issue was discussed with the EMA. The EMA confirmed on 6 February that no Direct Healthcare Professional Communication (DHPC) was required.

When writing to Otsuka Europe, the Authority asked it to consider the requirements of Clauses 2, 9.1 and 29 of the Code.

**RESPONSE**

Otsuka Europe stated that communications to its EU affiliates in relation to Jinarc SPC revisions had caused confusion resulting in the Jinarc SPC published on eMC from 15 February 2019 to 1 March 2019 containing the addition of gout but not the preceding revision, the addition of blister wallet cards.

Otsuka Europe stated that the current UK prescribing information for Jinarc (which contained both the addition of blister wallet cards and gout) was, from 15 February 2019 to 1 March 2019, inconsistent with the SPC available on the eMC. Otsuka UK followed the relevant EU process (EU-SOP-MA-002) and its own local process for updating the eMC (OPUK-SOP-RA-001) (copies of the SOPs were provided); the issue was the lack of clarity in the communications from Otsuka Europe in relation to the SPC revisions.

Although Otsuka Europe did not consider that the omission of the blister wallet cards in the SPC was a patient safety issue, the inconsistency amounted to a failure to maintain high standards, in breach of Clause 9.1 and a breach of the undertaking provided in Case AUTH/3041/6/18, in breach of Clauses 29 and 2.

The email sent by Otsuka Global Regulatory Affairs Region Europe on 26 February 2019 did not follow the relevant process in that it was from Global Regulatory Affairs Region Europe only, it did not contain all of the required attachments, and it caused confusion in the affiliates. Causing confusion in a communication formally notifying affiliates about a revision to a SPC amounted to a further failure to maintain high standards, contrary to the requirements of Clause 9.1. Otsuka Europe also considered that causing such confusion was a breach of the undertaking given in Case AUTH/3123/11/18, in breach of Clauses 29 and 2.

Otsuka Europe explained that the version of the SPC (uploaded to the eMC on 4 January) contained the blister wallet card revision, and was replaced on the eMC on 15 February 2019 with the version of the SPC that contained the gout revision but not the blister wallet revision; this was then replaced on the eMC by the consolidated SPC (containing blister wallet and gout revisions) on 1 March 2019. As noted in Otsuka's previous letter, a word version of the SPC was required in order to update the eMC, and this was only provided to Otsuka UK on 27 February 2019. Otsuka Europe provided a timeline to illustrate events.

As noted in Otsuka Europe's previous letter of 12 March 2019, when two or several stand-alone variation applications were being submitted and/or assessed in parallel at the EMA, the procedures would be kept separate. So, in this case it was not possible to avoid having an SPC with gout that did not contain the blister wallet cards. However, if this had been made clear to affiliates when the blister wallet card was approved, they could have planned how to deal with this, for example, by taking advice from the PMCPA.

The lack of clarity in relation to the communication of the various SPC revisions was subject to an open investigation and Otsuka Europe was considering how such communications could be improved in the future. In addition, Otsuka Europe was investigating why the communication of the consolidated SPC did not follow the relevant process.

As Otsuka Europe noted in its letter of 12 March 2019, it had communicated a mistake in the packaging and release of the Jinarc package leaflet at the manufacturing site in the UK where the previous version of the package leaflet was packaged with the product. The manufacturing site was notified on 12 October 2018 of an upcoming revision to the package leaflet with an implementation date of 30 November 2018. That package leaflet revision contained three updates:

- extended contraindication (hypersensitivity to benzazepine or benzazepine derivatives)
- missing adverse drug reaction 'abdominal pain' ('belly pain' in package leaflet)
- missing extension of indication (chronic kidney disease stage 1 to 4 instead of 1 to 3).

The manufacturing site mistakenly used the previous version of the package leaflet starting 30 November 2018. Otsuka identified the issue on 10 January 2019; between the 10 January and 18 February 2019 the manufacturing site identified the same issue in 14 batches (6 UK batches), of which 12 (4 UK batches) were released between 17 December 2018 and 7 February 2019 to avoid out-of-stock situations. Otsuka notified EMA and the Defective Medicines Report Centre (DMRC) at MHRA on 17 January 2019.

On 24 January 2019 EMA requested preparation of a DHCP letter and confirmed that an out-of-stock situation for Jinarc would have a wider implication for safety than release of the product with a superseded package leaflet. EMA agreed

that the batches should not be recalled but further replenishment of stock with the correct package leaflet should be initiated as soon as possible.

On 6 February 2019, EMA confirmed that no DHCP letter was required.

**PANEL RULING**

The Panel noted Otsuka Europe's submission that there had been two parallel revisions to the Jinarc SPC (addition of blister in wallets cards with new marketing authorization numbers and addition of gout as a common adverse drug reaction) and that the two revisions were each subject to separate applications to the EMA and therefore a combined consolidated version also had to be approved by the EMA.

The Panel noted Otsuka Europe's submission that there was a Jinarc SPC available on the eMC from 15 February to 1 March which contained the addition of gout but not the preceding SPC revision of addition of blister wallet cards and that the UK prescribing information current at that time which contained both the addition of gout and blister wallet cards was therefore inconsistent with the SPC published on the eMC during that time.

The Panel noted, based on Otsuka Europe's submission, that when two or more variation applications were submitted and/or assessed in parallel by the EMA, the procedures were kept separate, and further noted Otsuka Europe's submission that, in this case, having an SPC with gout but without the preceding blister wallet cards revision was unavoidable. However, the Panel noted Otsuka Europe's submission that the communication to the affiliates dated 14 February regarding this matter could have been clearer so they could have planned how to deal with this situation, and that the communication regarding the consolidated SPC sent to the affiliates on 26 February had not followed the relevant SOP including that it did not have all the required attachments and it was from Global Regulatory Affairs Region Europe only and that it caused confusion in the affiliates.

The Panel considered that the lack of clear communication by Otsuka Europe to its affiliates, which was compounded by the failure to follow, and lack of consistent application of, the relevant SOP, meant that Otsuka Europe had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted Otsuka Europe's admission regarding the breach of undertakings given in Cases AUTH/3041/6/18 and AUTH/3123/11/18.

The Panel noted that a form of undertaking and assurance was an important document. Companies had to give an undertaking that the material or activity in question and any similar material/activity, if not already discontinued or no longer in use, would cease forthwith and give an assurance that all possible steps would be taken to avoid similar breaches of the Code in future (Paragraph 7.1 of the Constitution and Procedure). It was very important for the reputation of the industry that companies complied with undertakings.

In its response Otsuka Europe explained that the omission of the blister wallet cards in the SPC whilst not a patient safety issue was an inconsistency with the prescribing information that amounted to a failure to maintain high standards in breach of the undertaking given in Case AUTH/3041/6/18.

The Panel noted that in Case AUTH/3041/6/18, Otsuka Europe was found in breach of: Clause 4.1 for promotional materials either missing prescribing information or not containing the latest version of the prescribing information, Clause 9.1 for Otsuka Europe's governance of materials falling below acceptable standards, and Clause 2 for, *inter alia*, not providing prompt communication to Otsuka UK regarding SPC updates and poor governance which the Panel had considered had potential safety implications. Although there was some overlap between Case AUTH/3041/6/18 and the current case, the Panel noted that there were important differences. The subject matter of the former did not include the accuracy of communications about SPC updates in relation to Jinarc. In addition, the Panel noted that whilst Case AUTH/3041/6/18 included the failure to include the latest version of prescribing information on materials, in the current case, Case AUTH/3169/3/19, the situation was somewhat unusual as from 15 February 2019 to 1 March 2019 the prescribing information included the addition of blister wallet cards and gout whereas the SPC published on the eMC during that time omitted blister wallet cards. The voluntary admission in Case AUTH/3169/3/19 did not refer to use of materials with the incorrect prescribing information. The Panel therefore considered, on balance, that the subject matter of the current case was sufficiently different to Case AUTH/3041/6/18 such that there was no breach of the undertaking given in that case. The Panel therefore ruled no breach of Clause 29 and Clause 2 in this regard.

In relation to the admission of a breach of undertaking and Case AUTH/3123/11/18 Otsuka Europe referred to the email for Global; Regulatory Affairs Region Europe dated 26 February 2019 and failure to follow process and causing confusion. In Case AUTH/3123/11/18, Otsuka Europe was found in breach of, *inter alia*, Clause 9.1 for lack of clear and consistent instructions to employees and third parties in relation to SPC changes and Clause 2 for its failure to timely and robustly address inadequacies in this process. The Panel considered that Otsuka Europe's breach of Clause 9.1 for the lack of clear communication to its affiliates and lack of consistent application of the relevant SOP as noted above in the current case (Case AUTH/3169/3/19) meant that it had breached the undertaking given in Case AUTH/3123/11/18. The Panel therefore ruled a breach of Clause 29. The Panel considered that Otsuka Europe's breach of undertaking meant that it had brought discredit upon, and reduced confidence in, the pharmaceutical industry and a breach of Clause 2 was ruled.

The Panel noted Otsuka Europe's admission in relation to an out-of-date package leaflet being

packaged with Jinarc at the manufacturing site. The Panel noted Otsuka Europe's submission that the manufacturing site was notified on 12 October 2018 of an upcoming revision to the leaflet with an implementation of 30 November 2018 but it mistakenly used the previous version. The Panel considered that Otsuka Europe had been let down by its manufacturing site. The Panel considered that the package leaflet was an important document for patients and such an error meant that Otsuka Europe had failed to maintain high standards and a breach of Clause 9.1 was ruled. The Panel considered that a breach of Clause 2 was a sign of particular censure. The Panel noted that Otsuka Europe had liaised with the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) with regard to this error and noted the actions Otsuka Europe submitted that it had agreed with the EMA on the matter. The Panel considered that, in these particular circumstances, and on balance, no breach of Clause 2 was warranted.

**Complaint received** **12 March 2019**

**Case completed** **5 July 2019**

# HEALTH PROFESSIONAL v NOVARTIS

## Presentation at Speaker Meeting

**An anonymous, contactable health professional who described themselves as a general practitioner complained about a presentation on Entresto (sacubitril and valsartan) delivered by a local consultant cardiologist at an event organised and sponsored by Novartis Pharmaceuticals UK. Entresto was indicated for the treatment of adults with symptomatic chronic heart failure with reduced ejection fraction.**

**The complainant alleged that the presentation on heart failure and Novartis' new product, Entresto, was not fair or balanced. Only the positive attributes of the medicine were presented and the audience was not given any information about potential side-effects or adverse reactions. In the complainant's view, the presentation was not sufficient such as to allow him/her to form his/her own opinion of the value of the medicine.**

**The detailed response from Novartis is given below.**

**The Panel noted that the meeting was designed to explore the 'myth of clinical stability in heart failure', the local burden of the condition and its impact on clinical resources. The Panel noted the timings and summarised content of the three presentations as set out in Novartis' response.**

**The first presentation discussed the economic burden of heart failure and the heart failure audit and did not mention Entresto. The second presentation 'Diagnosis and Management in Primary Care' discussed, *inter alia*, the causes, local prevalence, investigation and education and lifestyle management of heart failure. The treatment section discussed, *inter alia*, angiotensin receptor blockers, ACE inhibitors, beta blockers and mineralocorticoid receptor antagonists. Comparative efficacy and adverse event data for Entresto versus enalapril from PARADIGM-HF (McMurray *et al* (2014)) was discussed in 5 slides (3 efficacy, 1 adverse event and 1 summary slide). Four slides, each referenced to the Entresto summary of product characteristics, covered the practical prescribing of Entresto including initiating therapy, contraindications, dosing and special populations.**

**The third presentation, which appeared to be the subject of the complaint, titled [New York Heart Association] NYHA class and clinical outcomes in heart failure focussed on stratifying risk in patients with heart failure including patients with milder symptoms. The Panel noted Novartis' submission that this presentation referred to McMurray *et al* as that study contained data on the associated risks of sudden death between NYHA classes. The Panel noted that the presentation also included promotional claims and the final bullet point of the final slide 'Take home messages', in relation to sacubitril/valsartan and NYHA class read 'patients with NYHA class II symptoms should [be] switched if otherwise appropriate'.**

**The Panel also noted the safety findings in McMurray *et al* and that fewer patients stopped their study medication overall or because of an adverse event in the Entresto group than in the enalapril group. The authors noted that because of its greater vasodilator effects, treatment with Entresto was associated with a higher rate of symptomatic hypotension but there was no increase in discontinuation due to possible hypotension related adverse events.**

**The Panel noted that the presentation in question did not refer to potential side-effects or adverse reactions as stated by the complainant. The preceding presentation included some adverse event data from McMurray *et al* and information on contraindications and special populations from the SPC.**

**On balance, the Panel considered that the primary message of the presentation in question concerned NYHA classification and most of the data from McMurray *et al* was presented in that context. The complainant had not identified precisely what side effects/adverse reactions he/she considered were missing from the presentation in question. In this regard the Panel noted that the complainant bore the burden of proof. It was not for the Panel to infer such matters. The Panel therefore ruled no breach of the Code.**

An anonymous, contactable health professional who described him/herself as a general practitioner complained about a presentation on Entresto (sacubitril and valsartan) delivered by a local consultant cardiologist at an event organised and sponsored by Novartis Pharmaceuticals UK Ltd. Entresto was indicated for the treatment of adults with symptomatic chronic heart failure with reduced ejection fraction.

**COMPLAINT**

The complainant alleged that the presentation on heart failure and Novartis' new product, Entresto, was not fair or balanced, in breach of Clause 7.2. Only the positive attributes of the medicine were presented and the audience was not given any information about potential side-effects or adverse reactions. In the complainant's view, the presentation was not sufficient such as to allow him/her to form his/her own opinion of the value of the medicine.

**RESPONSE**

Novartis stated that the promotional speaker meeting in question took place in 2019 at a named

venue; it started at 6:15pm and ended at 9pm. Three health professionals were engaged to present at the meeting:

- The meeting chair delivered a 15 minute introductory presentation which focussed on the economic burden of heart failure and then discussed some of the key findings within the National Heart Failure Audit 2016/2017. This presentation was non-product specific and did not contain any element of promotion of Entresto.

- The second presentation (45 minutes) on 'Diagnosis and Management in Primary Care' contained an illustration of a variety of treatment options (slide 30 onwards). Entresto was discussed within this section as a treatment option among others, and the efficacy and safety of Entresto were discussed: specifically 5 slides focussed on efficacy and 6 slides focussed on safety. With specific regard to the safety slides, the presentation outlined information from the clinical trial PARADIGM-HF (McMurray *et al* (2014)) and included practical advice for prescribing Entresto, special populations and contraindications.

- The third presentation (45 minutes) was on 'NYHA [New York Heart Association] Classes and Clinical Outcomes in Heart Failure'. The presentation focussed on using NYHA classes to stratify risk in patients with heart failure and highlighted the risk to those patients with milder symptoms. As PARADIGM-HF contained data on the associated risks of sudden death between NYHA classes, the presentation included subgroup data from this trial to support the delivery of this message.

The presentations were delivered together in the order stated above so as to ensure an organic overview of heart failure and related treatments, including Entresto. To this end, the third presentation was purposefully delivered after the second presentation, so as to provide an objective and unambiguous panorama of the wider topic subject matter of the meeting and ensure the required balance to the information provided.

The speakers were engaged in light of their expertise in cardiology. Details were outlined in the relevant meeting approval form. As indicated on that form, the objectives for this meeting were:

> '1) Upskill local clinicians on the burden of heart failure in the community, (2) Identification, referral and management of heart failure and (3) Benefits of Entresto vs ACE inhibitors for heart failure.'

The invitation/agenda clearly outlined what would be presented at the meeting:

> 'We invite you to be part of the heart failure conversation. During this meeting we will explore the myth of clinical stability in heart failure, the burden of the condition in your locality and its impact on clinical resources. We will debate how to improve patient outcomes and raise awareness of the unmet needs of patients in a constantly changing NHS.'

The invitation/agenda contained the Entresto prescribing information.

Novartis stated that the meeting was promotional with a strong educational focus, it was attended by 12 health professionals, all of whom arrived within the first 10 minutes of the start of the meeting and stayed to the end. Therefore, all attendees were present for the delivery of all the presentations and were able to receive both the safety and efficacy data presented throughout the entirety of the meeting. Furthermore, the prescribing information for Entresto was included at the end of the second and third presentations and was also available in hard copy format at the meeting.

In summary, Novartis submitted that the content shared at the meeting, including information on Entresto, was fair and balanced and not in breach of Clause 7.2.

**PANEL RULING**

The Panel noted that according to its agenda the meeting was designed to explore the 'myth of clinical stability in heart failure', the local burden of the condition and its impact on clinical resources. The Panel noted the timings and summarised content of the presentations as set out in Novartis' response.

The Panel noted that the complainant's allegation was in relation to the third presentation.

The first presentation discussed the economic burden of heart failure and the heart failure audit and did not mention Entresto. The second presentation was titled 'Diagnosis and Management in Primary Care' and discussed, *inter alia*, the causes, local prevalence, investigation and education and lifestyle management of heart failure. The pharmacology treatment section began at slide 30 and discussed, *inter alia*, angiotensin receptor blockers, ACE inhibitors, beta blockers and mineralocorticoid receptor antagonists. Comparative efficacy and adverse event data for Entresto versus enalapril from PARADIGM-HF (McMurray *et al* (2014)) was discussed in 5 slides (3 efficacy, 1 adverse event and 1 summary slide). Four slides, each referenced to the Entresto summary of product characteristics, covered the practical prescribing of Entresto including initiating therapy, contraindications (7 listed), dosing and special populations (elderly, renal impairment and hepatic impairment).

The Panel noted that the third presentation which appeared to be the subject of the complaint was titled NYHA class and clinical outcomes in heart failure which focussed on using NYHA classes to stratify risk in patients with heart failure including patients with milder symptoms. The Panel noted Novartis' submission that this presentation referred to McMurray *et al* as that study contained data on the associated risks of sudden death between NYHA classes. The Panel noted that the presentation went

beyond stratifying risk in certain heart failure patients; it also included promotional claims and the final bullet point of the final slide titled 'Take home messages', in relation to sacubitril/valsartan and NYHA class read 'patients with NYHA class II symptoms should [be] switched if otherwise appropriate'.

The Panel noted Entresto's use in special populations, its contraindications, special warnings and precautions for use, interactions and undesirable effects as set out in its SPC. The Panel also noted the safety findings in McMurray *et al* and the study authors' statement that fewer patients stopped their study medication overall or because of an adverse event in the Entresto group than in the enalapril group. The study authors noted that because of its greater vasodilator effects, treatment with Entresto was associated with a higher rate of symptomatic hypotension but there was no increase in discontinuation due to possible hypotension related adverse events.

The Panel noted that the presentation in question did not refer to potential side-effects or adverse reactions as stated by the complainant. The preceding presentation included some adverse event data from McMurray *et al* and information on contraindications and special populations from the SPC.

On balance, the Panel considered that the primary message of the presentation in question concerned NYHA classification and most of the data from McMurray *et al* was presented in that context. The complainant had not identified precisely what side effects/adverse reactions he/she considered were missing from the presentation in question. In this regard the Panel noted that the complainant bore the burden of proof. It was not for the Panel to infer such matters. The Panel therefore ruled no breach of Clause 7.2 of the Code.

**Complaint received** **14 March 2019**

**Case completed** **17 September 2019**

# HEALTH PROFESSIONAL v NOVARTIS

## Provision of a meeting attendance certificate

**An anonymous contactable health professional complained that no attendance certificates were available following a meeting organised and sponsored by Novartis Pharmaceuticals UK Ltd.**

**In an email subsequent to the event, the representative asked when might be a suitable time to come and see the complainant with his/her certificate and an evaluation form. The representative was unable to email the certificate. The complainant responded by suggesting that the representative drop the certificate at the surgery reception, however, the representative replied by stating he/she was unable to do so on the day that he/she was happy to meet the complainant. The complainant stated that the representative had not given a time when the certificate would be dropped off which was inconvenient and inconsiderate. The complainant now awaited Novartis' reply to his/her suggestion that the certificate be posted.**

**The detailed response from Novartis is given below.**

**The Panel noted that following the meeting, the representative wrote to the complainant to arrange a face-to-face meeting for the delivery of the attendance certificate and evaluation form. The email stated that the representative was unable to email the certificate and was hoping the health professional was available for him/her to provide the certificate and to get feedback on the meeting. The Panel noted Novartis' submission that when it was no longer possible to meet on the agreed date the representative simply advised that he/she would drop off the attendance certificate at a future date, without mentioning the previously agreed meeting or asking for a new one.**

**In the Panel's view, whilst the representative's initial email should have been clearer that the health professional was not obliged to see the representative in order to obtain the attendance certificate, the follow-up communication was clearer in that regard. According to the email trail, the representative did not object to, or resist, the health professional's request that the certificate be left at reception. The Panel, therefore, considered that, on balance, the delivery of the attendance certificate was not an inducement to gain an interview and no breach was ruled.**

An anonymous contactable health professional complained on 12 March about the provision of a meeting attendance certificate associated with an event organised and sponsored by Novartis Pharmaceuticals UK Ltd earlier in March.

**COMPLAINT**

The complainant noted that no attendance certificates were available following the meeting and alleged that an email subsequently received from a representative was in breach of Clause 15.3. The email read:

> 'I am getting in touch with you today to ask when may be a suitable time to come and see you with your certificate and an evaluation form? Unfortunately, I am unable to send the certificate via email and am hoping that you may have some availability for me to give it to you and get some feedback on the meeting?'

The complainant stated that he/she responded by suggesting that the representative drop the certificate at the surgery reception, however, the representative replied by stating he/she was unable to do so on the day that he/she was happy to meet the complainant. The complainant stated that the representative had not given him/her a time when the certificate would be dropped off which was inconvenient and inconsiderate. The complainant had now suggested that the certificate was posted and he/she awaited Novartis' reply.

**RESPONSE**

Novartis understood that the representative in question and a health professional exchanged emails about the delivery of a meeting attendance certificate. They agreed to a face-to-face meeting for that purpose. Due to conflicting commitments on both sides, the meeting had to be cancelled and the attendance certificate could not be delivered on the agreed date. The representative thus offered to deliver the certificate at the next available opportunity, with no mention of the previously agreed meeting nor a request for a new meeting.

No other conversation about the matter, in writing or otherwise, took place between the representative and the health professional. In light of the above, Novartis considered that no inducement or subterfuge had been used to obtain an interview and there had not been a breach of Clause 15.3.

Novartis provided details about the meeting which was a company-organised promotional speaker meeting. No attendance certificates were available at the meeting and attendees were advised that representatives would provide hard copy certificates after the meeting.

Novartis outlined the email conversation between the representative and the complainant:

- On 8 March the representative wrote to the complainant to agree a mutually convenient date for a face-to-face meeting for the delivery of the attendance certificate and the evaluation form to collect feedback on the meeting.

- On the same day, the complainant replied and indicated that Wednesday, 13 March was a possible option.

- The representative replied to agree for a time for the visit.

- On 10 March, the complainant advised that he/she was no longer available on 13 March and asked for the certificate to be left at the surgery.

- On 12 March, the representative replied saying he/she was no longer able to drop the certificate off on the Wednesday; he/she gave no specific reason, but it was because of a supervening work commitment at the Novartis offices, which was advised with just two days' notice, on 11 March.

The representative advised that he/she would deliver the attendance certificate at the next possible opportunity; he/she did not ask or mention to meet the complainant face-to-face.

- On the same day, the complainant replied, asking for the date of delivery of the attendance certificate and suggested, alternatively, that it be posted to his/her home address.

Novartis stated that communications between the representative and the complainant clearly reflected the absence of any inducement or subterfuge to obtain an interview. The representative asked whether the complainant would be available for a meeting for the delivery of the attendance certificate and the collection of feedback on the meeting and the complainant agreed. When it was no longer possible to meet on the agreed date – for the reasons outlined above – the representative simply advised that he/she would drop off the attendance certificate at a future date, without mentioning the previous agreed meeting or asking for a new one.

Novartis understood that on the same day of this last communication, 12 March, the PMCPA received the complaint. In Novartis' view, such chronology of events appeared to be inconsistent with the ongoing conversations between the representative and the complainant. No further communication had occurred, and the attendance certificate had not yet been sent to the complainant.

Novartis stated that with regard to attendance certificates in general, its policy was to provide hard copies to meeting attendees and not email them. The representative followed this process; he/she recently completed training to ensure understanding of, and compliance with, the approval process for delivery of certificates of attendance. Novartis stated, however, that it now intended to review the process and add the email option for attendees' convenience.

The above said, to further improve its meetings and ensure that attendees could maximize the benefits while reducing any inconvenience, Novartis would ensure that attendance certificates were available in ample quantity at each meeting so that every attendee could receive one on the day.

Novartis stated that the content and tone of the communication was always appropriate and professional, the representative's intent was clear and direct; to deliver the attendance certificate at a time and in a manner best suited to the complainant, in compliance with the Code and Novartis' internal procedures.

In light of the above, Novartis denied a breach of Clause 15.3 and submitted that this was simply a case of a misunderstanding.

**PANEL RULING**

The supplementary information to Clause 15.3 Items Delivered by Representatives, stated that reply paid cards which referred to representatives delivering items to health professionals or other relevant decision makers, should explain that there was no obligation to grant the representative an interview when the items were delivered. This was to avoid the impression that there was such an obligation, which would be contrary to Clause 15.3 which prohibited the use of any inducement or subterfuge to gain an interview. In the Panel's view, the same principle applied to the delivery of an attendance certificate.

The Panel noted that following the meeting, the representative wrote to the complainant to arrange a face-to-face meeting for the delivery of the attendance certificate and evaluation form. The email stated that the representative was unable to email the certificate and was hoping the health professional was available for him/her to provide the certificate and to get feedback on the meeting. The Panel noted Novartis' submission that when it was no longer possible to meet on the agreed date the representative simply advised that he/she would drop off the attendance certificate at a future date, without mentioning the previously agreed meeting or asking for a new one.

The Panel noted Novartis' submission that, with regard to attendance certificates in general, its policy was to provide hard copies to meeting attendees and not email them. The Panel noted that this was covered in the Peer to Peer Handbook internal briefing document which also included a post-meeting checklist. The checklist asked 'Have you booked in a follow up Face to Face with the customers who attended?'. The Panel queried whether representatives might be encouraged to use delivery of the attendance certificate to ensure a follow-up meeting in this regard. The Panel noted Novartis' submission that it intended to review the process and add the email option for attendees' convenience and would take appropriate action to ensure that attendance certificates were available in ample quantity at each meeting so that every attendee could receive one on the day.

In the Panel's view, whilst the representative's initial email dated 8 March should have been clearer that the health professional was not obliged to see the representative in order to obtain the attendance certificate, it appeared from the follow-up communication dated 12 March that

the health professional was not obliged to see the representative in order to obtain his/her attendance certificate. According to the email trail, the representative did not object to, or resist, the health professional's request that the certificate be left at reception. The Panel, therefore, considered that, on balance, the delivery of the attendance certificate was not an inducement to gain an interview and no breach of Clause 15.3 was ruled.

**Complaint received** **12 March 2019**

**Case completed** **12 September 2019**

# ANONYMOUS v SANDOZ

## Conduct of a representative

**An anonymous health professional complained about the questions asked of the speakers by a Sandoz medical science liaison (MSL) at a Sandoz-sponsored meeting. Sandoz marketed the biosimilars Zessly (infliximab) and Hyrimoz (adalimumab).**

**The complainant explained that in February 2019, he/she attended an educational event run by Sandoz in Glasgow and connected to a venue in London via a video link. The event was advertised as non-promotional and health professionals spoke about diseases, treatment and therapeutic drug monitoring. The meeting ended with a multidisciplinary panel discussion from some of the remaining speakers. The purpose of the discussion was for attendees to ask the speakers more in depth questions. There were no questions from the audience so the Sandoz representatives asked questions. The complainant stated that he/she was concerned about the motive behind one of the named representative's questioning. The representative asked questions about switching and biosimilars such as how to do a successful switch, and then went on to mention therapeutic drug monitoring and how important it was. Upon discussions with his/her colleagues, the complainant had learned that Sandoz offered free therapeutic drug monitoring with some of its biosimilars. In that regard the complainant alleged that the representative had tried to influence the attendees into doing biosimilar switching and in turn switching to a Sandoz biosimilar due to the therapeutic drug monitoring offerings.**

**The detailed response from Sandoz is given below.**

**The Panel noted Sandoz's submission that it made funding available for therapeutic drug monitoring (TDM) services for its infliximab and adalimumab products on a reactive basis only. Its availability was not publicised and there was no proactive offer of the service. Sandoz submitted that while TDM was included as a topic on the agenda there was no mention at any time of Sandoz's involvement in the provision or funding of TDM services.**

**The Panel noted that the stated purpose of the meeting titled 'Biologics and co-morbidities in Autoimmune Disease: What can we learn from each other?' was to facilitate discussion around the approaches to patient management within the different therapy areas, to gain insight into co-morbidities and other challenges faced by health professionals who managed patients with autoimmune diseases and prescribed biologic therapies.**

**The Panel noted that the therapeutic drug monitoring presentation was delivered by an independent scientist and discussed drug levels in relation to infliximab and adalimumab, immunogenicity and measurement platforms. The presentation did not refer to funding or Sandoz's position on reactive funding. The Panel noted that other presentations during the day also referred to TDM, for example, the specialist gastro pharmacist's presentation on his/her role in biologics referred to TDM studies with infliximab and adalimumab. None of the presentations referred to Sandoz's position on reactive funding for TDM services for its biosimilars infliximab and adalimumab. The Panel noted that a nurse requested to change his/her presentation to 'How to implement biosimilars' which Sandoz agreed to; this presentation referred to infliximab and adalimumab but made no specific reference to Sandoz's biosimilars, Zessly and Hyrimoz.**

**The Panel noted that at the question and answer session at the end of the meeting, according to Sandoz, neither the panel nor the audience asked questions and thus the MSLs chairing the meeting asked a number of questions. The Panel noted that the MSL in question asked 4 questions and only the fourth question referred to therapeutic drug monitoring. The MSL's fourth question referred to a clinician who was '… really invested in things like TDM and levels and TNF …' and referred to the pressure across all specialities to use anti-TNF first line due to cost and queried whether, due to the potential for an immune shift, if it was always the best biologic to choose, finishing by asking the panel what practice they used to select a biologic and if they agreed with using anti-TNF first line due to its cost.**

**The Panel noted that the question at issue focussed on anti-TNF biologics and that there were many biosimilars within that class. The Panel did not consider on the evidence before it that the MSL in question had tried to influence attendees to switch to a Sandoz biosimilar due to its therapeutic drug monitoring offerings as alleged. In that regard, the therapeutic drug monitoring had not been referred to by the MSL as an inducement to prescribe and the Panel ruled no breach of the Code.**

**The Panel considered that the complaint solely concerned the questions asked by the MSL. Given its ruling and comments above the Panel considered that the fourth question which referred to therapeutic drug monitoring did not constitute a disguised promotional activity and no breach was ruled. Similarly given its comments and rulings above the Panel did not consider that either the company or the MSL had failed to maintain high standards in this regard and no breach of the Code was ruled including Clause 2.**

An anonymous health professional complained about the questions asked of the speakers by a Sandoz medical science liaison (MSL) at a Sandoz-sponsored meeting. Sandoz marketed the biosimilars Zessly (infliximab) and Hyrimoz (adalimumab).

**COMPLAINT**

The complainant explained that in February 2019, he/she attended an educational event run by Sandoz in Glasgow and connected to a venue in London via a video link. The event was advertised as non-promotional and health professionals spoke about diseases, treatment and therapeutic drug monitoring. The meeting ended with a multidisciplinary panel discussion from some of the remaining speakers. The purpose of the discussion was for attendees to ask the speakers more in depth questions. There were no questions from the audience so the Sandoz representatives asked questions. The complainant stated that he/she was concerned about the motive behind one of the named representative's questioning. The representative in question had asked questions about switching and biosimilars such as how to do a successful switch, and then went on to mention therapeutic drug monitoring and how important it was. Upon discussions with his/her colleagues, the complainant had learned that Sandoz offered free therapeutic drug monitoring with some of its biosimilars. In that regard the complainant considered that the representative had tried to influence the attendees into doing biosimilar switching and in turn switching to a Sandoz biosimilar due to the therapeutic drug monitoring offerings.

When writing to Sandoz the Authority asked it to consider the requirements of Clauses 2, 9.1, 12.1, 15.2 and 18.1.

**RESPONSE**

Sandoz stated that the meeting in question, 'Biologics and Co-morbidities in Autoimmune Disease: What Can We Learn from Each Other?', was a medical educational, non-promotional event which it had initiated, organised and funded. The arrangements for the meeting were approved through the Sandoz internal compliance system and the event was hosted at two sites (Glasgow and London), with an audience and speakers at both sites. An audio-visual link between the two venues allowed the audience at either site to see and hear all presentations during the day. The event was run by the medical function, the only commercial involvement was on the day logistical support. The speakers were external health professionals and one scientist who all had relevant experience within the therapeutic areas being discussed. The chairs at both sites were Sandoz medical science liaisons (MSLs). A transcript of the question and answer session referred to by the complainant was provided.

The non-promotional meeting was intended to facilitate discussion around the approaches to patient management within the different therapy areas, and to gain insight into the co-morbidities and other challenges faced by health professionals who managed patients with autoimmune diseases and prescribed biologic therapies. Health professionals invited to the meeting were from dermatology, rheumatology and gastroenterology. There were a number of co-morbidities that spanned these different therapy areas, and there were already clinics set up jointly between the different specialities, although this approach was not consistently demonstrated. The objective of the meeting was to bring together doctors, nurses and pharmacists who worked in these therapy areas, to exchange information and best practice, with the aim of improving patient care.

Health professionals were told about the meeting initially by a 'Save the Date' item, which was sent out from November 2018, followed by an email or hard copy invitation distributed from January 2019, which included the proposed agenda. Both non-promotional items were certified and distributed by representatives and MSLs. The invitation offered the recipient further information by means of contacting the MSLs. The representatives' role in distributing the 'Save the Date' and invitation was limited to providing the item in a non-promotional interaction without any detailed discussion. More than 400 invitations were distributed across the relevant UK health professionals.

The agenda consisted of presentations by rheumatology, gastroenterology and dermatology consultants who provided an overview of the diseases in their specialty for which biologics were a treatment option, the assessment tools used to assess the diseases, the management and therapies used, and how they monitored response. This was followed by an overview of therapeutic drug monitoring (TDM) by a scientist employed as the clinical lead for laboratory immunology at a hospital trust. A specialist hospital pharmacist in gastroenterology then provided an overview of his/her role which included staff education, communicating with patients and interpreting the results of TDM.

There were a further 3 sessions by specialist nurses in dermatology, rheumatology and gastroenterology, who all had the initial brief to discuss their role in the clinic and managing co-morbidities and discuss a relevant case study. Two of the nurses presented on these topics. However, the specialist inflammatory bowel disease (IBD) nurse did not have time to prepare a presentation on the agreed topic ('Nurse experience of joined up approach in their trust') and so he/she proposed an alternative title and subject ('How to implement biosimilars') which he/she had previously presented (details provided). This change was proposed two weeks before the meeting in February. The medical team considered the suggestion and agreed that it was an acceptable alternative at this late stage. Although highly relevant to the attendees, the topic of biosimilars switching was not initially included in the agenda and its addition was due to the last minute request from the nurse. The team also suggested that the nurse provided information on the 'IBD Passport' which was an online resource founded by him/her.

This was an entirely independent website that provided practical information for health professionals and was thought to be a useful topic to present at the meeting.

The final part of the meeting was a multidisciplinary panel discussion and question and answer session, scheduled for 1 hour.

This agenda did not change from the planning stage, except for the change noted above. A copy of the agenda and the certificate were provided.

An MSL chaired each meeting (Glasgow and London) and a medical advisor also attended the London meeting as an observer. Both sites had two external agency staff to provide the audio-visual link between the two sites, film and record the session. A representative provided logistical support at each site due to the number of attendees (details provided). Sandoz provided details of who had attended each meeting together with a copy of the certified briefing material provided to the representatives before they attended the meeting.

Sandoz explained that the representative referred to by the complainant was an MSL who directly reported to the medical director. The MSL's role was entirely non-promotional. As stated above, the meeting was initiated, organised and funded by the medical function at Sandoz, and an MSL chaired the meeting at each location. This involved opening the meeting, providing 'housekeeping' information (eg timings), introducing the speakers and chairing the Q&A session, scheduled for the last hour of the meeting.

During the Q&A session at the end of the meeting, neither the panel nor audience asked any questions initially. In their role as meeting chairs, the MSLs asked the panel a number of questions. These were not briefed before the meeting or prepared in advance but were asked as a direct result of the presentations and discussions during the day. Stimulating debate and encouraging audience participation was an established practice by those who chaired meetings and the MSLs considered at the time that this was required of them, as on the agenda, there was an hour set aside for this discussion.

- Sandoz summarised the topic of each of the four questions asked by the MSL Glasgow, which Sandoz understood formed the basis of the complaint (to provide context) and provided the full transcript of the questions as they were asked at the meeting. They included a question on data package for approval and whether there was a justification to require data on neutralizing and non-neutralizing anti-bodies; a question on whether gastroenterologists were concerned that biosimilars might be launched with no data on gastroenterology indications; a question on likelihood of the National Institute for health and Care Excellence (NICE) guidelines becoming more aligned with EU requirements rather than current requirement for strict adherence to disease activity scores (DAS) before biologic prescription; and a question on how biologics were selected for first line use.

The MSL role was the field-based element of Sandoz's medical affairs department. It provided a non-promotional service to health professionals that facilitated interactions and scientific discussions on relevant therapy areas. The employee in question had been trained on the Code and participated in ongoing Code educational activities. His/her role profile and Code training certificates were provided.

Sandoz explained that TDM was increasingly seen as an important tool in the management of patients on biologic treatments, especially within gastroenterology. NHS Scotland funded TDM in patients on infliximab and adalimumab, but across the rest of the UK availability was variable. Pharmaceutical companies were a well-established source of funding for these services and in that regard Sandoz funded TDM services for its infliximab and adalimumab products on a reactive basis only. Its availability was not publicised and the service was not offered proactively. Only if requested or enquired about would the availability of the service be discussed. Further details on this were provided in a medical briefing and the terms of the TDM reactive provision of funding to trusts was also defined in a template contract agreement (copies provided).

While TDM was included as a topic on the agenda of the meeting, Sandoz's involvement in the provision or funding of TDM services was not discussed.

Sandoz noted that the complaint related specifically to the questions asked by an MSL set out above. It was clear from the questions that there was no basis for two of the complainant's central assertions: that the MSL asked the panel questions about switching and biosimilars such as how to do a successful switch and that he/she then went onto mention therapeutic drug monitoring and how important it was.

Sandoz stated that it had reviewed the questions to determine whether the MSL had tried to influence the attendees into doing biosimilar switching and in turn switching to a Sandoz biosimilar due to the therapeutic drug monitoring offerings as alleged.

The first question was a technical question, which related to regulatory data requirements. It was clear from the outset that the question applied equally to biosimilars and originators, and this was explicitly stated. There is nothing in the question which could be considered an attempt to influence attendees into switching to biosimilars. There was no mention of either any Sandoz product or therapeutic drug monitoring.

The second question related to the lack of data available for biosimilars in gastroenterology and how this might be a concern for professionals and patients. Since this was clearly a drawback in prescribing biosimilars it contradicted the assertion that the representative had tried to influence the attendees into biosimilar switching. No mention was made in this question of either any Sandoz product or TDM.

The third question was about the differences between NICE and the EU approach to treatment pathways. There was no mention of biosimilar, any Sandoz product or TDM.

The final question was the only one which referred to TDM. In this question, the representative commented on the appeal of anti-TNF biologics as a first line treatment due to their 'cheapness' and queried whether that was always best, noting that 'it might not always be the best biologic to go to'. On consideration of this question, the complainant's interpretation was not supported.

Sandoz addressed the elements of the complaint individually.

> '…trying to influence the attendees into doing biosimilar switching…'

The question did not specifically mention either biosimilars or originators.

The question focused on anti-TNF biologics. There were many available biosimilars in this class. However, a reference to anti-TNF biologics clearly could not be taken to refer exclusively to biosimilars and not originators. Reference was made to the 'cheapness' of anti-TNF biologics. While their price could be in part attributed to the availability of biosimilars, anti-TNF biologics were comparatively 'cheap' as a class, including originators.

Moreover, the representative in this question queried whether the practice of using this class, which contained a comparatively high number of biosimilars, as a first line treatment was in fact the correct course. This directly contradicted the complainant's contention that the representative had tried to influence the attendees into doing biosimilar switching.

> '…and in turn switching to a Sandoz biosimilar….'

As above, there was no support for the assertion that any attempt was made to influence attendees into switching to any biosimilar. No reference was made to any Sandoz product. Sandoz noted that it was not the only manufacturer of anti-TNF biosimilars, and so referring to anti-TNF biologics was not a disguised reference to Sandoz products.

> '…due to the therapeutic drug monitoring offerings.'

The final question asked by the representative was the only question, which mentioned TDM. The reference was brief and incidental ('[name] who's really invested in things like TDM …') and could not be considered an inducement to change prescribing or other behaviour.

Sandoz similarly refuted any contention that the mere mention of TDM in the question was improper. As noted above, TDM was a topic on the agenda for the meeting, and a presentation was made by an independent specialist. There was no mention, at any time, of Sandoz's involvement in the provision or funding of TDM services. The fact that the complainant stated that it was upon discussion with his/her colleagues that he/she learned that Sandoz offered free therapeutic drug monitoring, further reinforced that this was not discussed or mentioned during the meeting.

With regard to Clause 12.1, Sandoz submitted that there was no promotional content or any information that could be deemed disguised promotion in any of the presentations or as part of the Q&A session. Sandoz products were not mentioned. There was no reference to Sandoz's funding for TDM or encouragement to switch to Sandoz biosimilars. Sandoz did not consider that either the materials used during the meeting, or its intent, were promotional. The presentations were created by the external speakers (and only reviewed and certified by Sandoz to ensure they were in line with the requirements of the Code). The Q&A, as demonstrated by the transcript provided, had no promotional content.

The conduct of all Sandoz attendees demonstrated a high standard of ethical conduct and complied with all relevant requirements of the Code. Representatives were only involved in a logistical capacity, and there was no specific mention of any Sandoz-branded products. Sandoz submitted that the transcript made clear that the MSLs maintained a high standard of ethical conduct, and it did not consider that the complainant had provided any evidence that this was not the case. The company denied a breach of Clause 15.2.

Sandoz stated that there was no pecuniary benefit offered, promised or implied to the attendees as an inducement to prescribe. The complainant alleged that TDM was mentioned in such a way as to influence the attendees to switch to Sandoz biosimilars on the basis of the free TDM service offered. The only mention of TDM from the MSLs was in passing, as one of the things that a specialist in the field was 'invested in'. The inclusion of a presentation on TDM was unrelated to service provision. That Sandoz could fund TDM was not mentioned. The fact that the complainant learnt that Sandoz did offer free TDM upon discussion with his/her colleagues reinforced that this was not discussed or mentioned during the meeting. The provision of TDM by the company was clearly defined and was offered as part of a package deal as has been described.

Sandoz submitted that high standards were maintained at all times in the preparation and execution of the meeting. The objective to promote a better understanding of the three therapy areas was clear from the outset. The totality of evidence provided supported this assertion. The company denied a breach of Clause 9.1.

The meeting in question was a non-promotional, educational meeting with the sole aim of providing relevant education and cross specialism perspectives for health professionals working in auto-immune diseases. The meeting had not brought discredit upon, or reduced confidence in, the industry.

Attendees gave very positive feedback and noted the value of this type of event.

Sandoz reiterated that the meeting was an educational, non-promotional, medical meeting, which sought to bring together different specialties, where there were a number of co-morbidities that required joint working with the ultimate aim of providing better care for patients. There was no intention or evidence that the meeting was set up to promote any of Sandoz products, or to tell the delegates about reactive funding of TDM from Sandoz to try and persuade them to prescribe a Sandoz product.

Maintaining the highest standards of compliance was very important to Sandoz and it took any complaints seriously and had used this as an opportunity to rigorously examine its practices.

**PANEL RULING**

The Panel noted Sandoz's submission that it made funding available for TDM services for its infliximab and adalimumab products on a reactive basis only. Its availability was not publicised and there was no proactive offer of the service. Sandoz submitted that while TDM was included as a topic on the agenda there was no mention at any time of Sandoz's involvement in the provision or funding of TDM services.

The Panel noted that the stated purpose of the meeting titled 'Biologics and co-morbidities in Autoimmune Disease: What can we learn from each other?' was to facilitate discussion around the approaches to patient management within the different therapy areas, to gain insight into co-morbidities and other challenges faced by health professionals who managed patients with autoimmune diseases and prescribed biologic therapies. The Panel noted that the meeting was scheduled to start at 9am and finish at 5pm and, according to the agenda, the day began with 3 presentations in each of rheumatology, dermatology and gastroenterology including an overview of the diseases and their management and therapies for which biologics were a treatment option. There followed an Overview of Therapeutic Drug Monitoring followed by a presentation on the role of the specialist gastro pharmacist in biologics and 3 sessions by specialist nurses in dermatology, rheumatology and gastroenterology respectively to discuss their role and a relevant case study. The latter nurse changed the content of his/her presentation at a late stage to 'How to implement biosimilars'. The day concluded with the multi-disciplinary panel discussion and Q&A.

The Panel noted that the therapeutic drug monitoring presentation was delivered by an independent scientist and discussed drug levels in relation to infliximab and adalimumab, immunogenicity and measurement platforms. The presentation did not refer to funding or Sandoz's position on reactive funding. The Panel noted that other presentations during the day also referred to TDM, for example, the specialist gastro pharmacist's presentation on his/her role in biologics referred to TDM studies with infliximab and adalimumab. None of the presentations referred to Sandoz's position on reactive funding for TDM services for its biosimilars infliximab and adalimumab. The Panel noted that, as referred to above, a nurse requested to change his/her presentation to 'How to implement biosimilars' which Sandoz agreed to; this presentation referred to infliximab and adalimumab but made no specific reference to Sandoz's biosimilars, Zessly and Hyrimoz.

The Panel noted that at the question and answer session at the end of the meeting, according to Sandoz, neither the panel nor the audience asked questions and thus the MSLs who were chairing the meeting asked a number of questions. The Panel noted that the MSL in question asked 4 questions and only the fourth question referred to therapeutic drug monitoring. The MSL's fourth question referred to a clinician who was '... really invested in things like TDM and levels and TNF ...' and referred to the pressure across all specialities to use anti-TNF first line due to cost and queried whether, due to the potential for an immune shift, if it was always the best biologic to choose, finishing by asking the panel what practice they used to select a biologic and if they agreed with using anti-TNF first line due to its cost.

The Panel noted that the question at issue focussed on anti-TNF biologics and that there were many biosimilars within that class. The Panel did not consider on the evidence before it that the MSL in question had tried to influence attendees to switch to a Sandoz biosimilar due to its therapeutic drug monitoring offerings as alleged. In that regard, the therapeutic drug monitoring had not been referred to by the MSL as an inducement to prescribe and the Panel ruled no breach of Clause 18.1 of the Code.

The Panel considered that the complaint solely concerned the questions asked by the MSL. Given its ruling and comments above the Panel considered that the fourth question which referred to therapeutic drug monitoring did not constitute a disguised promotional activity and no breach of Clause 12.1 was ruled. Similarly given its comments and rulings above the Panel did not consider that either the company or the MSL had failed to maintain high standards in this regard and no breach of Clauses 15.2 and 9.1 were ruled. The Panel consequently ruled no breach of Clause 2.

**Complaint received** **18 March 2019**

**Case completed** **18 September 2019**

**CASE AUTH/3174/3/19**

# ANONYMOUS EMPLOYEES v OTSUKA EUROPE

## Conduct of Otsuka Europe

**A 'group of concerned employees' complained about the arrangements for international meetings and comments made by a senior Otsuka Europe employee at an internal meeting.**

**The detailed response from Otsuka Europe is given below.**

**The complainants alleged that previous international meetings had been misclassified and certified as non-promotional events when it was clear that such activities were promotional. The complainants alleged that these had been classified incorrectly due to commercial pressure to get more attendees for non-promotional meetings. Such activities were disguised promotion as health professionals thought they were attending a non-promotional meeting as part of an exchange of scientific material. One example was a symposium at the 2018 European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) Congress. The symposium had been certified as non-promotional when in fact it was promotional.**

**These concerns had been highlighted to the compliance department, but no action had been taken, probably because no-one was well versed with the ABPI Code, and Otsuka Europe had to rely on a third party for most of its compliance activities.**

**The Panel noted Otsuka Europe's submission that the symposium was led by the medical department and was classified as non-promotional in the approval system. Otsuka Europe stated that its investigation identified that the symposium slides were approved by the country of the congress affiliate (Denmark) as promotional.**

**The Panel noted Otsuka Europe's submission that on review of the symposium slides it was clear to the company that it was promotional and disguised in that regard; it discussed treatment with tolvaptan (Jinarc marketed by Otsuka) which according to Otsuka Europe was the only medicine licensed for the indication. The Panel noted Otsuka Europe's submission that the materials used to advertise the symposium all referred to a discussion of the ERA-EDTA guidelines on Autosomal Dominant Polycystic Kidney Disease (ADPKD), which were in fact guidelines on the use of tolvaptan in ADPKD.**

**The Panel noted that the symposium slides included multiple references to tolvaptan. It was difficult for the Panel to understand how Otsuka could have classified and treated this meeting as anything but promotional. It had been classified as promotional by the Danish affiliate. In this regard, the Panel ruled a breach of the Code as Otsuka Europe had failed to maintain high standards.**

**In the Panel's view, it was clear that the symposium was an Otsuka Europe promotional symposium. However, the Panel considered that, on the balance of probabilities, not all health professionals, based on the materials used to advertise the symposium at the scientific congress, would have expected the symposium to be a promotional meeting. In that regard it was disguised promotion and a breach was ruled as acknowledged by Otsuka Europe.**

**The Panel noted that Otsuka Europe had identified a number of other issues during its investigation into this matter including, *inter alia*, the symposium slides not being consistent with the tolvaptan SPC and lack of prescribing information. Whilst the Panel was extremely concerned with regard to the issues identified, there had been no allegation on these points and therefore the Panel could make no rulings.**

**Whilst the Panel was concerned that Otsuka Europe classified a clearly promotional symposium as non-promotional, it did not consider that, on balance, the particular circumstances of this case warranted a ruling of a breach of Clause 2 and ruled accordingly. The complainants appealed this ruling.**

**The Appeal Board noted that the symposium at issue was led by Otsuka Europe's medical department and was classified as non-promotional in the approval system. The Appeal Board noted that the symposium slides included multiple references to tolvaptan. The symposium slides were approved as promotional by the Danish affiliate. In addition, Otsuka Europe had a promotional booth for Jinarc (tolvaptan). The Appeal Board agreed with the Panel in that it was difficult to understand how the symposium in question could have been anything other than promotional.**

**The Appeal Board noted Otsuka Europe's submission that its investigation indicated that the company did not properly understand the distinction between promotional and non-promotional activities as defined by the Code and this failure was at an organisational level. Otsuka Europe submitted that it was not conscious misclassification of non-promotional meetings, but gross incompetence caused by a lack of training, management and support. Otsuka Europe submitted that these failings had reduced confidence in the pharmaceutical industry.**

**The Appeal Board considered that such failings reduced confidence in the pharmaceutical industry and ruled a breach of Clause 2 as acknowledge by the company. The appeal on this point was successful.**

**The Appeal Board noted the issues found during Otsuka Europe's investigation and the actions taken. It noted that some of these were identified**

**in the recent audits of Otsuka Europe and Otsuka UK required in Cases AUTH/3041/6/18 and AUTH/3123/11/18.**

**The complainants provided information about an internal company meeting held in March. It was a weekly management update meeting that focused on the Appeal Board meeting on 13 March. There was a debrief on the presentation and the types of questions asked by the Appeal Board.**

**The complainants stated that attendees were informed that culture was of particular interest, especially around whistleblowing. A senior employee at Otsuka Europe (named) went on to add that during this 'period' it was very easy to finger point individuals and departments. This person then stated that there might be some individuals in the audience that wondered what he/she was still doing in the organisation.**

**The complainants alleged that the senior employee then asked all present to raise their right hand and swear that they would not complain about individuals or departments to anyone for the next 6 months. He/she added that when staff were questioned during the PMCPA audit, they had to be careful with their answers. The PMCPA would open up with easy questions, and then tackle more difficult areas, eg were we happy with the processes and the organisation? He/she hinted that staff would receive training to indicate their appropriate answers.**

**The complainants alleged that, in summary, they should not be holding each other to account (by swearing not to complain) and would receive training to provide the answers the PMCPA want to hear during the audit (lack of transparency).**

**The complainants alleged that it was clear that the culture in Otsuka Europe was going from bad to worse and they did not see it improving imminently.**

**The complainants provided a copy of an email (22 March) to staff following the meeting on 18 March which suggested that even the leadership team felt that the pledging episode was not appropriate. The complainants wanted to find out what specific feedback had been received from the leadership team, and if a formal investigation had begun (especially as this had been brought to the attention of the PMCPA).**

**The complainants believed that the email was not entirely accurate (the complainants stated that they did not know what would be communicated to the PMCPA). Before making all of the employees pledge that they would not complain, he/she shared a restaurant motto – 'If you are happy tell everyone, if you are not tell us'. This action was to stop disgruntled employees from going outside the company to complain about certain issues. The complainants believed with the restaurant story in mind and the forced pledging, the direct message was not to further whistle blow.**

**The complainants stated that, given this evidence, the senior employee conceded that he/she was not clear with his/her messaging and that his/her actions caused certain employees to feel deeply uncomfortable.**

**It was not entirely clear to the Panel what exactly was said at the meeting in question. The Panel noted the interview notes with some of the meeting attendees who were also on the leadership team.**

**The Panel noted that the comments were made at a meeting which was to inform staff that Otsuka UK and Otsuka Europe would be audited by the Authority later that year. The audit was in relation to three cases and in each case it appeared that the complainant was an Otsuka employee. The Panel further noted that at the time of the meeting in question there were ongoing Otsuka cases at the Authority where the complainant appeared to be an anonymous employee or employees. The Panel considered that it was a critical time for the company with regard to compliance and comments made by senior members of staff at this time would be fundamental in driving the company's compliance culture.**

**The Panel considered, based on the evidence before it, that the comments made at the meeting in question would, on the balance of probabilities, have been interpreted by some as saying do not complain outside the company. In the Panel's view, such comments from a senior employee would have a huge impact on the culture within the company at a critical time when the company ought to be actively encouraging open dialogue about compliance matters. The Panel considered that Otsuka Europe had therefore failed to maintain high standards and a breach was ruled as acknowledged by the company.**

**In the Panel's view, the implied message 'do not complain outside the company' was a serious matter that undermined the Code and self-regulation. Regardless of whether or not such a message was intended or misinterpreted, the Panel considered that the comments at the meeting in question meant Otsuka Europe had brought discredit upon and reduced confidence in the pharmaceutical industry. The Panel therefore ruled a breach of Clause 2.**

**With regard to the allegation in relation to training staff to ensure that appropriate answers are given during the upcoming audit, the Panel noted Otsuka Europe's submission that audit readiness training for employees would focus on what to expect and would convey the importance of answering questions completely and honestly. Otsuka Europe made no submission about whether such matters were within the scope of the Code. The Panel noted that it was not inappropriate to provide training in preparation for an audit. The training had not taken place at the time of the complaint. The complainants had not shown that their concerns gave rise to a Code matter. No detail was provided. The Panel ruled no breach of the Code as the subject matter of complaint was outside the scope of the Code.**

A 'group of concerned employees' complained about the arrangements for international meetings and comments made by a senior Otsuka Europe employee at an internal meeting.

**1 International meetings**

**COMPLAINT**

The complainants alleged that it had come to their attention that previous international meetings had been misclassified and certified as non-promotional events when it was clear that such activities were promotional. The complainants alleged that these had been classified incorrectly due to commercial pressure to get more attendees for non-promotional meetings.

The complainants alleged that such activities were disguised promotion as health professionals thought they were attending a non-promotional meeting as part of an exchange of scientific material. One such example was the 2018 European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) Congress symposium, which had been certified as non-promotional when in fact it was promotional.

The complainants stated that these concerns had been highlighted to the compliance department, but no action had been taken, probably because none of the compliance personnel in Otsuka Europe was well versed with the Code, and Otsuka Europe had to rely on a named third party for most of its compliance activities.

When writing to Otsuka Europe, the Authority asked it to bear in mind the requirements of Clauses 2, 9.1 and 12.1.

**RESPONSE**

Otsuka Europe submitted that the meeting that the complainant referred to was the European Renal Association – European Dialysis and Transplant Association congress which took place in Copenhagen, 24-27 May 2018. A concern about the 2018 ERA-EDTA congress was identified to European Compliance on 7 March 2019, and an internal incident stating that the 2018 ERA-EDTA Otsuka-sponsored symposium discussed the use of Jinarc (tolvaptan) in Autosomal Dominant Polycystic Kidney Disease (ADPKD) which was 'coded' as non-promotional was raised. An investigation commenced on 8 March and would be completed no later than 19 April 2019. The investigation identified that the slides used at the symposium were approved by the local affiliate for Denmark as promotional; the investigation did not review the Denmark job bags but a quick search confirmed that the local affiliate consistently treated the symposium and its materials as promotional.

Otsuka Europe submitted that its presence at this congress was a promotional booth for Jinarc and a symposium. Neither Otsuka Europe nor Otsuka UK took UK health professionals to the congress but a presentation sourced from the ERA-EDTA website indicated 279 of the registered attendees at the congress were from the UK (there were 9,598 participants in total).

The Otsuka Europe symposium was led by the medical function and was classified as non-promotional in the Otsuka Europe approval system. The certified programme for the symposium submitted to the meeting organisers noted that the objectives of the symposium were:

- Present the latest scientific data, and ensure health professionals understand the diagnosis and treatment/management of rapid progression in patients with ADPKD
- Raise awareness of the need for regular follow up, investigations and early treatment
- Discuss the ERA-EDTA guidelines and their practical application
- Present case studies – challenging cases that could require early intervention.

Otsuka Europe submitted that on review of the slides presented at the symposium it was clear that the entire symposium was in fact promotional and disguised in that regard, as it discussed treatment with tolvaptan (which was the only medicine licensed for this indication), in breach of Clause 12.1. In addition, various material used to advertise the symposium all referred to a discussion of the ERA-EDTA guidelines on ADPKD, which were in fact guidelines on the use of tolvaptan in ADPKD.

Otsuka Europe submitted that during the investigation in to this complaint, other issues were identified. These included:

- Misclassification of other materials as non-promotional that were, in fact, promotional (for example the various materials used to advertise the symposium as noted above, the videos of the presentations which were intended to be placed on the ERA-EDTA website after the congress). Otsuka Europe considered that these materials were also in breach of Clause 12.1, and that this amounted to a failure to maintain high standards, in breach of Clause 9.1.

- Content in the presentations which, when viewed correctly as promotional activity, was not consistent with the particulars of the SPC, specifically:

    - 'How to start tolvaptan – patient toolkit' where the speaker stated 'Take the first pill at ~6am in the morning …' where Section 4.2 of the SPC stated 'The morning dose is to be taken at least 30 minutes before the morning meal' and later '… (45 mg taken upon waking and prior the morning meal …'.
    - 'How to start tolvaptan – patient toolkit' where the speaker stated 'Stop 4 weeks before trying to get pregnant' where the SPC listed pregnancy as a contraindication and Section 4.6 stated 'Women of childbearing potential must use adequate contraceptive measures during Jinarc use. Jinarc must not be used during pregnancy'.
    - Two slides indicate dosing which did not match Section 4.2 of the SPC. The SPC stated

'The initial dose is 60mg tolvaptan per day as a split-dose regimen of 45mg +15 mg …. The initial dose is to be titrated upward to a split-dose regimen of 90mg tolvaptan (60mg + 30mg) per day and then to a target split-dose regimen of 120mg tolvaptan (90mg + 30mg) per day, if tolerated, with at least weekly intervals between titrations'. It went on to state 'Patients may down-titrate to lower doses based on tolerability. Patients have to be maintained on the highest tolerable tolvaptan dose'. The presenter provided a bar graph indicating a dosage of 30 mg tolvaptan (15mg +15 mg) per day under the heading 'Target dose?' A possible polling slide included below a heading 'How should uptitration be done? Which answer do you consider most appropriate?' three options – 'All patients have to be uptitrated to 90/30 mg', which was inconsistent with 'Patients may down-titrate to lower doses based on tolerability' from the SPC; 'Seeing the data [sic] 45/15 mg is sufficient', which was inconsistent with this same statement from the SPC as well as its accompanying statement that 'Patients have to be maintained on the highest tolerable tolvaptan dose' and 'Uptitration should be the target, however, lower doses may be sufficient in case of problems' which was difficult to assess based on the lack of specificity in the latter part of the sentence.

Otsuka Europe submitted that it had not been asked to respond to the requirements of Clause 3.2 in relation to this case but considered that this amounted to a failure to maintain high standards, in breach of Clause 9.1.

Otsuka Europe submitted that:

- The presentations did not contain prescribing information and there was no indication that it was present at the symposium. Otsuka Europe had not been asked to respond to the requirements of Clause 4.1 in relation to this case, but the company considered that this amounted to a failure to maintain high standards, in breach of Clause 9.1.
- No formal certified speaker briefing for symposium speakers was developed although it appeared that there may have been an informal brief. Otsuka Europe considered that failing to formally brief speakers, in combination with the numerous other errors in relation to its congress participation amounted to a failure to maintain high standards, in breach of Clause 9.1.
- Certain promotional materials were not certified:
    - The signatory signed the incorrect part of the certificate for the item.
    - Further, one job bag (OPEL/0518/JIN/1282) was a medical information request form and therefore did not require certification; however, it was raised for certification and was not certified before use; additionally, the hard copy approval (which was also after first use) occurred before the certification.

Otsuka Europe stated that it had no explanation as to why many of the job bags were not certified correctly. It had not been asked to respond to the requirements of Clause 14.1 in relation to this case but considered that this amounted to a failure to maintain high standards, in breach of Clause 9.1.

The additional material used at the congress, including the promotional booth for Jinarc was provided.

Otsuka Europe stated that it recognized the seriousness of the issues identified and considered that it's approach to the symposium amounted to a failure to maintain high standards, in breach of Clause 9.1. Additionally, given the severity of the failings in relation to participation in this congress, it acknowledged a breach of Clause 2.

There were indications that as an organisation Otsuka Europe did not properly understand the distinction between promotional and non-promotional activities as defined by the ABPI Code. Reference was made to an extract from the 2018 brand plan for Jinarc; this categorisation was used for at least one other brand (Samsca). Otsuka Europe reviewed the presentation for both brand plans with a view to identifying the source of the mischaracterisation. Given that this failure appeared to be at an organisational level, this amounted to a failure to maintain high standards, in breach of Clause 9.1 and brought the industry in to disrepute, in breach of Clause 2.

With regards to the complainants' reference to 'commercial pressure to get more attendees for non-promotional meetings', it had no evidence as to whether this was the case for ERA-EDTA in 2018. However, as part of the investigation in to this complaint Otsuka Europe uncovered an email in relation to ERA-EDTA 2019 which indicated that there might have been such pressure (a comment in particular from a commercial employee which notes 'Clinicians are nowadays not interested in promotional Sympo, but want to talk about disease management, patient outcome and guidelines'). Otsuka Europe's participation in the congress in 2019 was cancelled.

As a result of these above issues as well an on-going case currently with the Panel (Case AUTH/3153/1/19), Otsuka Europe reviewed planned activities at congresses. Plans for Otsuka Europe presence at congresses in 2019 were requested from the brand teams and reviewed by Compliance using the following criteria:

- Has the process been correctly followed and sufficient time given for preparing the project?
- For projects initiated after 31 January 2019 (when the Concept Form was introduced), has a Concept Form been completed?
- Based on the documentation provided, did the meeting meet the expectations of the ABPI Code and/or local codes?

Otsuka Europe submitted that where there were identified issues with the preparation for a meeting and insufficient time to correct these, the company's presence at the congress had been cancelled. As part of this review, further misclassification of meetings as non-promotional had been identified and addressed.

Otsuka Europe submitted that based on this further misclassification, which was subsequent to the ABPI Code baseline training and European Regional SOP training provided in 2018 and 2019, the company had determined that compliance issues had not been remediated, and additional effort was necessary. Therefore, all Otsuka Europe initiated promotional and non-promotional activities, including the below (unless such activities were required for legal, regulatory (eg, prescribing information and risk minimisation materials) or contractual reasons were stopped. Work done jointly with Lundbeck would be subject to additional scrutiny and external signatory support might be used):

- Congresses
- Advisory boards
- Promotional material
- PR and advertising
- Interactions with patient advocacy groups
- Market research.

Otsuka Europe stated that it would only resume these activities once it was confident that they could be executed in compliance with the Code. In addition, it would review current brand plans as a matter of urgency to identify any similar issues and take appropriate action, as necessary.

Otsuka Europe stated that it was obvious it needed to retrain employees (including signatories) on the Code (including the distinction between promotional and non-promotional activities). Additionally, as employees had begun to work with the company's revised European Regional SOPs, their feedback indicated that they needed more specific detail in the documents. Therefore, it was conducting a comprehensive review of certain SOPs to obtain all feedback and would implement more specific SOPs to ensure employees had a level of direction that made them confident in their daily activities. Finally, a retrospective review of all external meetings from 2016 to current day was also planned to ensure that any additional issues could be identified and addressed.

In April, an employee raised a concern to compliance with regards to the ERA-EDTA guidelines on ADPKD that required an investigation. Otsuka Europe raised an incident and cross-linked it to an earlier, related complaint that was raised in March. Otsuka Europe would conduct the investigation and provide the PMCPA with the conclusion as it might have direct bearing on this case.

**PANEL RULING**

The Panel noted Otsuka Europe's submission that a concern regarding the Otsuka sponsored symposium at the 2018 ERA-EDTA congress in Copenhagen was raised internally prior to the Authority's receipt of the complaint.

The Panel noted Otsuka Europe's submission that the symposium was led by the medical department and was classified as non-promotional in the electronic approval system. Otsuka Europe stated that its investigation identified that the symposium slides were approved by the country of the congress affiliate (Denmark) as promotional.

The Panel noted the objectives of the symposium and that they referred to, *inter alia*, treatment/ management of Autosomal Dominant Polycystic Kidney Disease (ADPKD), the ERA-EDTA guidelines and case studies.

The Panel noted Otsuka Europe's submission that on review of the symposium slides it was clear to the company that it was promotional and disguised in that regard; it discussed treatment with tolvaptan (Jinarc marketed by Otsuka) which according to Otsuka Europe was the only medicine licensed for the indication. The Panel noted Otsuka Europe's submission that the materials used to advertise the symposium all referred to a discussion of the ERA-EDTA guidelines on ADPKD, which were in fact guidelines on the use of tolvaptan in ADPKD.

The Panel noted that the symposium slides included multiple references to tolvaptan. It was difficult for the Panel to understand how Otsuka could have classified and treated this meeting as anything but promotional. It had been classified as promotional by the Danish affiliate. In this regard, the Panel considered that Otsuka Europe had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted that the symposium slides stated, on the welcome and introduction slide, in small font, 'This meeting is organised and funded by Otsuka Pharmaceutical Europe Ltd'. The Panel further noted that this statement was on various materials used to advertise the symposium including the advertisement in the industry symposium booklet, the symposium invitation for electronic distribution, the flyer for distribution at the congress, room signage, poster board, banner stands and symposium booklet. These materials used to advertise the symposium made no mention of tolvaptan but referred to ADPKD and the ERA-EDTA guidelines which, according to Otsuka Europe, were guidelines on the UK of tolvaptan in ADPKD.

The Panel noted that promotional material did not have to be labelled as such but must not mislead in that regard. The Panel noted that at international congresses, it was not uncommon for companies to conduct both promotional and non-promotional activities and therefore health professionals must not be misled as to which activities were promotional and which were either non-promotional and/or the legitimate exchange of medical and scientific information during the development of a medicine.

In the Panel's view, it was clear that the symposium in question was an Otsuka Europe promotional symposium. However, the Panel considered, noting its

comments above, that, on the balance of probabilities, not all health professionals, based on the materials used to advertise the symposium at the scientific congress, would have expected the symposium to be a promotional meeting. In that regard it was disguised promotion and a breach of Clause 12.1 was ruled as acknowledged by Otsuka Europe.

The Panel noted that Otsuka Europe had identified a number of other issues during its investigation into this matter including, *inter alia*, the symposium slides not being consistent with the tolvaptan SPC and lack of prescribing information. Whilst the Panel was extremely concerned with regards to the issued identified, there had been no allegation on these points and therefore the Panel could make no rulings.

The Panel noted that Clause 2 was a sign of particular censure and reserved for such use. Whilst the Panel was concerned that Otsuka Europe classified a clearly promotional symposium as non-promotional, it did not consider that, on balance, the particular circumstances of this case warranted a ruling of a breach of Clause 2 and ruled accordingly.

**APPEAL BY THE COMPLAINANT**

The complainants alleged that it was clear that Otsuka Europe was unable distinguish between promotional and non-promotional activities. However, this was in part due to commercial pressure to certify such activities as non-promotional (as identified by Otsuka Europe). The internal investigation by Otsuka Europe did not complete by 19 April 2019 (no feedback was provided) – this was not an accurate representation by Otsuka Europe.

The complainants appealed the Panel's ruling of no breach of Clause 2.

The complainants alleged that this was a systemic problem within Otsuka for the following reasons:

- Conscious misclassification of non-promotional meetings.
- Failure to maintain high standards.

**RESPONSE FROM OTSUKA**

Otsuka Europe submitted that as acknowledged in its initial response to this case, it considered that this matter amounted to a breach of Clause 2. During the investigation conducted there was an indication that Otsuka Europe did not properly understand the distinction between promotional and non-promotional activities as defined by the Code and this failure was at an organisational level. This issue had recently been reinforced by a third party consultancy review of all Otsuka Europe meetings from 1 January 2016 which noted:

> 'We are concerned that the expectations of delegates accepting an invitation might be misguided as many of the events focus far more on Otsuka products than might be expected from the meeting titles and descriptions. This is particularly true for ADPKD meetings. Where the content is within label, these events should be regarded as promotional events.'

Otsuka Europe submitted that it was currently reviewing the information from the third party and would ensure that remediation activities were put in place to provide the necessary education and support in areas where concerns had been identified.

As noted by the Panel, it was difficult to understand how the symposium in question could have been anything other than promotional. Otsuka Europe considered this a systemic issue. This, combined with historical indications that there might have been commercial pressure to miscategorise such symposia as non-promotional, amounted to an activity that reduced confidence in the industry, and brought it into disrepute.

Otsuka Europe noted that the complainants stated that the investigation into the congress at issue in this case was not completed by the date proposed in the Otsuka Europe response (19 April 2019). This was correct. The investigation report was approved internally in June 2019. This delay was unacceptable and was attributable to a lack of capacity and a lack of leadership in certain areas. Information on action taken to address this appeared below.

Otsuka Europe submitted that whilst it acknowledged that the above amounted to a breach of Clause 2, it considered it vital that the Appeal Board understood the significant actions that had been taken in order to address these and the other issues faced by Otsuka Europe:

- Details of various staff changes and appointments were provided.
- As communicated to the PMCPA on 6 April 2019, Otsuka Europe had ceased initiating promotional and non-promotional activities unless such activities were required for legal, regulatory (eg, prescribing information and risk minimisation materials) or contractual reasons. The latter included work done jointly with Alliance partners. From June 2019, any Otsuka Europe signatories had to have completed comprehensive third party validation.
- A cross-functional project team had developed Otsuka Europe specific procedures for all Code-related activities conducted by Otsuka Europe, in order to provide the depth of detail required by the organisation. These had been extensively reviewed and were currently being cross-checked to ensure that they were robust. These would then be rolled out with comprehensive face-to-face training and knowledge and would then be validated via Otsuka's learning management system.
- The July meeting of the newly formed European Pharmaceutical Leadership Team (EPLT) included an assessment of the current challenges faced by Otsuka Europe, what the future held for the organisation and what the leadership team wanted, and how the leadership team intended to achieve their goals. Details were provided. These included:

  - Creation of a Vision and Roadmap to 2024.
  - Strategy to achieve Roadmap to 2024.

    - Continue to strengthen Culture & Engagement.
    - Continue CORE activities.
- Get the 'Basics' right on business processes.

The above goals were presented at a town hall meeting in July 2019.

- A European Code of Conduct for all employees that would set out the ethical standards for employees to adhere to was being developed.
- Otsuka Europe was committed to transparent communication within the organisation and expected the same from its leadership team. In addition to the weekly town hall meetings, Otsuka Europe had instituted weekly 'Ask EPLT' sessions where any staff member might ask questions as part of a small group in a more informal setting.

Otsuka Europe hoped that the above demonstrated the approach that Otsuka Europe was taking to address the significant issues that it faced.

**FINAL COMMENTS FROM THE COMPLAINANT**

The complainants acknowledged that Otsuka Europe accepted a breach of Clause 2. The complainants were surprised by the statement from the third party that had conducted a review of all Otsuka Europe meetings from 1 January 2016. If this had revealed that the issues in Otsuka Europe were widespread, surely all activities should have been stopped (material and activities were still carrying on), and all employees should undergo retraining immediately? The findings had not been shared. The complainants presumed that the reason for confidentiality was that Otsuka was still in the process of reviewing the report. The complainants advised Otsuka to share the learnings so that previous mistakes were not repeated.

The complainants urged Otsuka's current leadership to have more tangible outputs for those on the ground. The complainants stated that they did not see a significant difference between the past and present leadership.

**APPEAL BOARD RULING**

The Appeal Board noted that the symposium at issue was led by Otsuka Europe's medical department and was classified as non-promotional in the electronic approval system. The Appeal Board noted that the symposium slides included multiple references to tolvaptan. The symposium slides were approved as promotional by the Danish affiliate. In addition, Otsuka Europe had a promotional booth for Jinarc (tolvaptan). The Appeal Board agreed with the Panel in that it was difficult to understand how the symposium in question could have been anything other than promotional.

The Appeal Board noted Otsuka Europe's submission that its investigation indicated that the company did not properly understand the distinction between promotional and non-promotional activities as defined by the Code and this failure was at an organisational level. The representatives from Otsuka Europe submitted that it was not conscious misclassification of non-promotional meetings, but gross incompetence caused by a lack of training, management and support. Otsuka Europe submitted that these failings had reduced confidence in the pharmaceutical industry.

The Appeal Board considered that such failings reduced confidence in the pharmaceutical industry and ruled a breach of Clause 2 as acknowledge by the company. The appeal on this point was successful.

The Appeal Board noted the issues found during Otsuka Europe's investigation and the actions taken. It noted that some of these were identified in the recent audits of Otsuka Europe and Otsuka UK required in Cases AUTH/3041/6/18 and AUTH/3123/11/18.

**2 Internal meeting 18 March**

**COMPLAINT**

The complainants provided additional information about an internal company meeting held that day (18 March). It was a weekly management update meeting that focused on the Appeal Board meeting on 13 March. There was a debrief on the presentation and the types of questions asked by the Appeal Board.

The complainants stated that attendees were informed that culture was of particular interest, especially around whistleblowing. A senior employee at Otsuka Europe (named) went on to add that during this 'period' it was very easy to finger point individuals and departments. This person stated that there might be some individuals in the audience that wondered what he/she was still doing in the organisation, especially as the impression might be that he/she 'is no good/ an idiot' [sic] … given the numerous failings. This person announced that he/she was not 'going anywhere'.

The complainants alleged that the senior employee then asked all present to raise their right hand and swear that they would not complain about individuals or departments to anyone for the next 6 months. He/she added that when staff were questioned during the PMCPA audit, they had to be careful with their answers. He/she declared that the PMCPA would open up with easy questions, and then tackle more difficult areas, eg were we happy with the processes and the organisation? He/she hinted that staff would receive training to indicate their appropriate answers.

The complainants alleged that, in summary, they should not be holding each other to account (by swearing not to complain) and would receive training to provide the answers the PMCPA want to hear during the audit (lack of transparency).

The complainants alleged that it was clear that the culture in Otsuka Europe was going from bad to worse and they did not see it improving imminently.

The complainants provided a copy of an email (22 March) to staff following the meeting on 18 March which suggested that the leadership team felt that the pledging episode was not appropriate. The

complainants wanted to find out what specific feedback he/she received from the leadership team, and if a formal investigation had begun (especially as this had been brought to the attention of the PMCPA). The complainants believed that the email was not entirely accurate (the complainants stated that they did not know what would be communicated to the PMCPA). Before making all of the employees pledge that they would not complain, he/she shared a restaurant motto – 'If you are happy tell everyone, if you are not tell us'. This action was to stop disgruntled employees from going outside the company to complain about certain issues. The complainants believed with the restaurant story in mind and the forced pledging, the direct message was not to further whistle blow.

The complainants stated that, given this evidence, the senior employee conceded that he/she was not clear with his/her messaging and that his/her actions caused certain employees to feel deeply uncomfortable.

When writing to Otsuka Europe, the Authority asked it to bear in mind the requirements of Clauses 9.1 and 2 of the Code

**RESPONSE**

Otsuka Europe stated that the complainant was referring to the weekly management update meeting that took place on 18 March 2019. These meetings occurred every Monday as part of the commitment to employees to provide open, transparent communication and to update on progress on the CORE programme as well as other business updates. All Otsuka Europe employees and office based Otsuka UK and OEDC employees were invited to attend and the slides were made available on the intranet site for those who were unable to attend in person.

The CORE programme was a key initiative in Otsuka Europe aiming to improve processes, culture and how the different entities in Otsuka work together more effectively. The complainant referenced CORE as being a 'positive initiative' with 'more transparent communication'.

At the meeting on 18 March, the main agenda item was to update the organisation on the outcome of the Appeal Board that took place on 13 March. The employees were taken through the same slides that were used in the Appeal Board presentation on 13 March and were informed of the outcome that Otsuka Europe and Otsuka UK would be audited by the PMCPA in late June/early July and that both companies would receive a public reprimand.

Otsuka Europe submitted that the comments that the complainants referred to were taken out of context. Some of the comments quoted by the complainants were made but with a very different intention. As part of the CORE programme, there was as real focus on improving the culture in Otsuka Europe. The comments made around asking the audience to raise their right hands and pledge not to complain around others were simply made to try to promote an open culture of giving and receiving feedback to individuals and teams. An email was sent to all employees following the meeting (22 March) to clarify this. As part of the CORE programme, there was a work-stream focusing on Audit Readiness. The aim of this initiative was to ensure that Otsuka was audit ready at all times both for internal and external audits. It had been communicated to employees that they would be supported both before any such audits, during the audits and in the remediation post-audit. Employees were not told that they would 'receive training to indicate our appropriate answers'.

Otsuka Europe submitted that the communication at these meetings had been transparent at all times. It continued to execute its culture strategy and would provide audit readiness training for employees; this training would focus on what to expect from an audit (including that the interviews would be entirely confidential) and would convey the importance of answering questions completely and honestly.

In relation to the comments made by the senior employee at the meeting on 18 March, Otsuka Europe submitted that there had been no breach of Clauses 9.1 or 2.

In a further response following notification of the additional information from the complainants, some members of the leadership team fed back that the comments could have been misinterpreted by staff to mean do not complain outside of the company, or potentially do not complain. It was acknowledged that high standards had not been maintained, in breach of Clause 9.1 but there was not a breach of Clause 2.

**PANEL RULING**

The Panel noted the complainants' allegation that employees were asked to raise their right hand and swear that they would not complain about individuals or departments to anyone for the next 6 months. The Panel noted Otsuka Europe's submission that all Otsuka Europe employees, office-based Otsuka UK and OEDC employees were invited to attend the weekly management update meeting in question which was also placed on the intranet.

The Panel noted Otsuka Europe's submission that the comments referred to by the complainants were taken out of context and the company was trying to promote an open culture of giving and receiving feedback to individuals and teams.

It was not entirely clear to the Panel what exactly was said at the meeting in question. The Panel noted the interview notes with some of the meeting attendees who were also on the leadership team; these referred to the comments in question potentially being misinterpreted as saying to staff do not complain outside of the company and staff should not have been asked to do the pledge; and that the intention was not to say 'don't complain' but to say 'also discuss this with the person you have a concern with so that they have a chance to change their behaviours/actions', but this could have been misinterpreted.

The Panel noted that the comments were made at a meeting which was to inform staff that Otsuka UK and Otsuka Europe would be audited by the Authority later that year. The audit was in relation to three cases and in each case it appeared that the complainant was an Otsuka employee. The Panel further noted that at the time of the meeting in question there were ongoing Otsuka cases at the Authority where the complainant appeared to be an anonymous employee or employees. The Panel considered that it was a critical time for the company with regard to compliance and comments made by senior members of staff at this time would be fundamental in driving the company's compliance culture.

The Panel considered, based on the evidence before it, that the comments made by a senior employee at the meeting in question would, on the balance of probabilities, have been interpreted by some as saying do not complain outside the company. In the Panel's view, such comments from a senior employee would have a huge impact on the culture within the company at a critical time when the company ought to be actively encouraging open dialogue about compliance matters. The Panel considered that Otsuka Europe had therefore failed to maintain high standards and a breach of Clause 9.1 was ruled as acknowledged by the company.

The Panel noted that the email sent on 22 March, following the company's notification of the complaint, to the attendees to apologise that his/her pledge request and the intended message might not have been clear to all. The email further stated that there were complaint mechanisms such as the Speak Up line run by a third party which protected anonymity.

In the Panel's view, the implied message 'do not complain outside the company' was a serious matter that undermined the Code and self-regulation. Regardless of whether or not such a message was intended or misinterpreted, the Panel considered that the comments at the meeting in question meant Otsuka Europe had brought discredit upon and reduced confidence in the pharmaceutical industry. The Panel therefore ruled a breach of Clause 2.

With regard to the allegation in relation to training staff to ensure that appropriate answers are given during the upcoming audit, the Panel noted Otsuka Europe's submission that audit readiness training for employees would focus on what to expect and would convey the importance of answering questions completely and honestly. Otsuka Europe made no submission about whether such matters were within the scope of the Code. The Panel noted that it was not inappropriate to provide training in preparation for an audit. The training had not taken place at the time of the complaint. The complainants had not shown that their concerns gave rise to a Code matter. No detail was provided. The Panel ruled no breach of the Code as the subject matter of complaint was outside the scope of the Code.

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|---|---|
| **Complaint received** | **20 March 2019** |
| **Case completed** | **16 October 2019** |

**CASE AUTH/3176/3/19**

# COMPLAINANT v ORION PHARMA

## Email and website

**A complainant who described him/herself as a concerned UK health professional complained about an email from Orion Pharma UK, sent via a named healthcare publication. The email urged recipients to watch a video on 'Medicines optimisation and the clinical challenges in respiratory care'. It was stated at the top of the email that 'This campaign has been produced by [a named healthcare publisher] with funding from Orion Pharma'.**

**The complainant stated that the email contained promotional information but no prescribing information. The email linked directly to the respiratory academy website which was sponsored by Orion (amongst others). The complainant alleged that the website thanked its valued sponsors who provided arms-length funding to support running of the academy, although the website was designed according to Orion's products and was clearly being used by Orion as a promotional tool, however, it did not appear to be described as such and had no prescribing information.**

**The complainant alleged that Orion's email which intentionally pointed to the website demonstrated at least an extremely weak process and oversight and at most an intent to set up supposedly independent websites that could be used for promotional purposes.**

**The detailed response from Orion is given below.**

**The Panel did not consider that the email in question promoted any particular Orion medicine and thus no prescribing information or adverse event reporting statement was required. The Panel ruled no breaches of the Code in this regard.**

**The Panel noted that the email stated that the campaign had been produced by the healthcare publisher with funding from Orion. The Panel queried whether this was an accurate description noting Orion's submission that it had commissioned the healthcare publisher to design, create and market a series of key opinion led educational videos focussing on respiratory management. In the Panel's view, Orion was more involved in the video campaign than the declarations in the email implied. The Panel considered that Orion had failed to maintain high standards in this regard and ruled a breach of the Code in relation to the email.**

**The Panel noted that the complainant had not provided evidence to show that the respiratory academy website was promotional as alleged and the Panel therefore ruled no breach of the Code in this regard.**

**The Panel noted that the website stated that the video series, of which the video in question was a part of, was produced by the healthcare publisher with funding from Orion Pharma. In the Panel's view, Orion was more involved in the production of the videos, including the video at issue above, than the website implied, and the Panel therefore ruled a breach of the Code in relation to declarations on the website about Orion's involvement in the video campaign. Orion had failed to maintain high standards in this regard and a further breach of the Code was ruled.**

**Whilst the Panel had some concerns about the video, in its view, the complainant had not established that the video was promotional and thus that prescribing information, the adverse event reporting statement or date on which the material was last drawn up was required. The content of the video was not promotional and therefore it did not constitute disguised promotion. The Panel therefore ruled no breaches of the Code in this regard.**

**Whilst in the Panel's view the complainant had not established that the email or website were promotional, the Panel noted that both the video and email had been certified and therefore ruled no breach of the Code.**

**The Panel did not consider that the particular circumstances of this case were such as to warrant a breach of Clause 2 which was a sign of particular censure. No breach of Clause 2 was ruled.**

A complainant who described him/herself as a concerned UK health professional complained about an email (ORI5285v) from Orion Pharma UK Limited, sent via a named healthcare publication. The email urged recipients to watch a video on 'Medicines optimisation and the clinical challenges in respiratory care'. It was stated at the top of the email that 'This campaign has been produced by [a named healthcare publisher] with funding from Orion Pharma'.

**COMPLAINT**

The complainant stated that the email contained promotional information, although it was not clear what the promotional material was. There was no prescribing information.

The complainant stated that he/she had clicked on the link to see what the videos were. This linked directly to the respiratory academy website which was another asset created by the healthcare publisher; the academy was itself sponsored by Orion (amongst others). On the academy website the healthcare publisher thanked its valued sponsors, who provide arms-length funding to

support the running of the academy – although the complainant noted that the relationship was so close that the website was designed according to the products Orion had. This was clearly being used as a promotional tool by Orion – although on the website itself it did not appear to be described as such and had no prescribing information.

If the website was alone this could be a simple oversight but Orion's crafting of an email that intentionally pointed at the website that was supposedly separate, demonstrated at least an extremely weak process and oversight and at most an intent to set up supposedly independent websites that could then be used for promotional purposes.

With regard to the email itself, the complainant alleged breaches of Clauses 4.1, 4.2, 4.4, 4.6, 4.9 and 9.1. With regard to the linked website and contained videos, the complainant alleged breaches of Clauses 4.1, 4.2, 4.3, 4.4, 4.6, 4.8, 4.9, 9.1, 9.10, 12.1 and 14.1. Overall, the complainant alleged a breach of Clause 2.

Orion was asked to respond to the clauses cited by the complainant in relation to the 2016 Code.

**RESPONSE**

Orion stated that as part of its commitment to help improve patient care in respiratory management, it commissioned the healthcare publishers to design, create and market a series of key opinion led educational 'conversation-style' videos focussing on respiratory management entitled 'Medicines optimisation and the challenges'. Orion had clearly identified its sponsorship of this educational project and had declared involvement on all materials in line with the requirements of Clause 9.10.

The commissioned videos were designed to support health professional education, in particular for those with roles based in medicines management/practice-based pharmacists, GPs, nurses and commissioners; the videos were tailored to the needs of each group. As the videos were educational, each was associated with 0.5 CPD points.

The educational videos did not endorse the use of any specific product. This content was hosted within the clearly identifiable sponsored content section of the respiratory academy website and each video was clearly labelled as being sponsored by Orion. Orion had not placed any product promotional content on this platform. The educational content of the videos reflected the opinions of those involved, and Orion's only involvement was to fund the project and check that the content of the materials was consistent with the requirements of the Code. As such, the material was reviewed and certified by Orion, in accordance with its standard operating procedures. Accordingly, Orion maintained that the requirements of Clause 4 (and the sub-clauses cited by the complainant) did not apply; there was no requirement to provide prescribing information on educational resources that did not contain promotional content.

Email notifications alerting recipients to the availability of the educational videos were sent to users who had registered with the healthcare publication website. Registration required users to confirm whether they had read and understood the site privacy policy and whether they wished to opt-in to receiving electronic marketing content, which might contain promotional material including from pharmaceutical companies, and detailed how to unsubscribe.

Third party mailing lists were used to distribute sponsored content, such as the videos in question, within the academy health professional community, and required data subjects to opt-in. When signing up to newsletters or registering to attend an event, users were presented with the opportunity to update their third-party consent.

Orion noted that the email notification that was sent in this instance clearly identified that the campaign had been produced by the healthcare publisher with funding from Orion. Orion had made every effort to be clear and transparent and to alert recipients about the nature of its involvement, in line with Clause 9.10. The email notification went on to offer an explanation of the content of the video material available. Orion did not promote the use of any specific product as part of the email notification; the email offered a clear explanation of the educational content of the video resource, so there was no need to fulfil the requirements of Clause 4 (and associated subsections mentioned by the complainant) of the Code.

The academy website was independent from Orion. Orion was a corporate supporter of the academy commissioning platform, 2018-2019. Orion's involvement in this educational video series had been to sponsor an educational campaign that was hosted within this commissioning platform. In all cases, content sponsored by Orion was clearly identifiable.

Treatment choices were discussed in the videos but only in the broadest sense and no specific products were mentioned or endorsed. Orion had not promoted any particular product in association with this project and as no references were made to specific products in the video, Orion refuted the suggestion that the material was disguised promotion.

All material associated with the funding was reviewed and certified in accordance with company procedures and the requirements of the Code. Therefore, Orion maintained that it had met the requirements of Clause 14.1. Orion provided copies of the certificates for the email content and video mentioned by the complainant.

In summary, Orion submitted that the matters raised by the complainant were not representative of the way that it had sponsored this project. From investigations and knowledge of the organisation Orion was confident that the project it commissioned from the healthcare publisher had not been used as a promotional tool or linked in any way to the promotion or prescription of Orion medicines.

Orion submitted that it had been clear and transparent about its involvement with the sponsored educational materials available on the academy website. Users must opt-in to receiving emails that contained sponsored content and might update their consent on a project-by-project basis. Therefore, only those who opted in received the email in question.

The project sponsored the provision of materials with genuine educational content for the healthcare community, which aimed to optimise patient treatment through consideration of medicines optimisation in primary care. Orion was keen to support colleagues working in primary care and offered useful resources to help with medicines optimisation in the NHS, as such, the company considered that it had maintained high standards.

As a consequence, Orion did not consider that the email or sponsored video content in question, or the way they were offered to health professionals, were such as to bring discredit upon, or reduce confidence in, the industry and in that regard it denied a breach of Clause 2.

**PANEL RULING**

The Panel noted that the email in question sent from the named healthcare publication with the subject line 'Join the discussion: think before you prescribe' included in the body of the email the header 'This email has been sent by [named healthcare publication] and contains third party promotional information' followed in more prominent font by 'This campaign has been produced by [named healthcare publisher] with funding from Orion Pharma'. The email invited readers to watch and included a direct link titled 'Medicines optimisation and the clinical challenge in respiratory care' to a video which was hosted within the sponsored content section of a named respiratory academy website. This video was one of three videos within a series. All three videos had the same initial title 'Medicines optimisation and the challenges in respiratory care' and respectively covered the clinical perspective, commissioning perspective and the pharmacy perspective. The video linked to the email in question covered the clinical perspective. All three videos were hosted within the sponsored content section of the academy website and when one video was being viewed within a window on the website, the remaining two videos were available below the window to be selected and viewed.

The Panel noted Orion's submission that the e-mail notification regarding the availability of the educational video was sent to appropriately registered users of the healthcare publication website and third party mailing lists were used to distribute sponsored content, such as the video in question, within the respiratory academy healthcare professional community and required data subjects to opt-in.

The Panel noted that Clause 4.1 of the Code required prescribing information to be included in promotional material. Clause 4.2 listed the elements of the prescribing information required. Clause 4.4 required that in the case of digital material such as emails the prescribing information as required by Clause 4.1 might be provided either by inclusion in the digital material itself, or by way of a clear and prominent direct single click link. Clause 4.6 stated that in the case of promotional material included on the Internet, there must be a clear, prominent statement as to where the prescribing information can be found.

The Panel did not consider that the email promoted any particular Orion medicine and thus no prescribing information was required. The complainant had not provided evidence to the contrary. The Panel therefore ruled no breach of Clauses 4.1, 4.4 and 4.6 in relation to the email. The Panel noted that Clause 4.9 required that all promotional material must include the prominent statement 'Adverse events should be reported. Reporting forms and information can be found at [web address which links directly to the MHRA Yellow Card site]. Adverse events should also be reported to [relevant pharmaceutical company]'. The Panel noted its comments above and ruled no breach of Clause 4.9.

The Panel noted that the email notification identified that the campaign had been produced by the healthcare publisher with funding from Orion. The Panel queried whether this was an accurate description noting Orion's submission that it had commissioned the healthcare publisher to design, create and market a series of key opinion led educational videos focussing on respiratory management. In the Panel's view, Orion was more involved in the video campaign than the declarations in the email implied and the Panel considered that Orion had failed to maintain high standards in this regard and ruled a breach of Clause 9.1 in relation to the email.

The Panel noted that Clause 9.10 required that material relating to medicines and their uses, whether promotional or not, and information relating to human health or diseases which is sponsored by a pharmaceutical company must clearly indicate that it has been sponsored by that company. The supplementary information stated that the declaration of sponsorship must be sufficiently prominent to ensure that readers of sponsored material were aware of it at the outset. The wording of the declaration must be unambiguous so that readers would immediately understand the extent of the company's involvement and influence over the material. This was particularly important when companies were involved in the production of material which was circulated by an otherwise wholly independent party, such as supplements to health professional journals.

The Panel noted that the complainant had not provided evidence to show that the respiratory academy website was promotional as alleged and the Panel therefore ruled no breach of Clauses 12.1,14.1, 4.1, 4.3, 4.4, 4.6, 4.8 and 4.9.

The Panel noted that the complainant referred to the phrase which appeared on the sponsors page of the website 'We thank our valued sponsors, who provide arms-length funding to support the running of the Academy'. The Panel noted that directly

below this declaration it stated 'See below for a range of sponsored content that we have developed in collaboration with these organisations'. The sponsors page then listed the logos of four different pharmaceutical companies including Orion and at the bottom the page under the heading Sponsored content appeared links to the three videos described above stating sponsored by Orion and another item listed as being sponsored by another pharmaceutical company.

The Panel noted Orion's submission that it was a corporate sponsor of the academy website commissioning platform for 2018-2019. The Panel did not consider that the complainant had provided evidence to show that the statement 'We thank our valued sponsors, who provide arms-length funding to support the running of the Academy' did not reflect Orion's involvement with regard to the running of the academy. The Panel further noted, however, that a footer in very small print which seemed to appear on every page of the academy website including the sponsors page and the page to which the email was directed stated 'The [named academy] has been developed and is produced by [named healthcare publisher], the publisher of [named healthcare publications] working in partnership with [named academy]. All educational content for the website and roadshows has been initiated and produced by [named academy/named healthcare publisher]'. Three pharmaceutical company's logos including Orion's were included above the footer with the title Sponsors.

The Panel further noted that the website stated that the video series, of which the video in question was a part of, was produced by the healthcare publisher with funding from Orion Pharma. The Panel noted Orion's submission that its only involvement was the funding of the project and checking that the content of the materials was consistent with the requirements of the Code. The Panel queried whether this was accurate noting Orion's submission that it had commissioned the healthcare publisher to design, create and market a series of key opinion led educational videos focussing on respiratory management. In the Panel's view, Orion was more involved in the production of the videos, including the video at issue above, than the website implied and the Panel therefore ruled a breach of Clause 9.10 in relation to declarations about Orion's involvement in the video campaign including 'All educational content for the website and roadshows has been initiated and produced by [named academy/named healthcare publisher]' and 'This video series has been produced by [named healthcare publisher] with funding from Orion Pharma'.

The Panel noted that whilst the complainant referred to videos when listing the clauses he/she considered were in breach, the email provided by the complainant directed readers to one of the videos, 'Medicines optimisation and the challenges in respiratory care: A Clinical Perspective'. It was not for the Panel to make out a complainant's allegation and the Panel therefore considered the complaint in relation to the specific video referred to by the complainant.

Whilst the Panel had some concerns about the video, in its view, the complainant had not established that the video was promotional and thus that prescribing information, the adverse event statement or date on which the material was last drawn up was required. The Panel therefore ruled no breach of Clauses 4.1, 4.3, 4.4, 4.6, 4.8 and 4.9 in relation to the video in question.

In the Panel's view, and noting its comments above, the content of the video was not promotional, and therefore it did not constitute disguised promotion and thus no breach of Clause 12.1 was ruled.

The Panel noted that the complainant raised Clause 14.1 which required that promotional material must not be issued unless its final form, to which no subsequent amendments will be made, has been certified by one person on behalf of the company in the manner provided for by this clause. Whilst in the Panel's view the complainant had not established that the email or website were promotional, the Panel noted that both the video and email had been certified as general promotional material under the product 'Corporate' by Orion. The Panel therefore ruled no breach of Clause 14.1.

The Panel noted its ruling of a breach of Clause 9.10 above and considered that Orion had failed to maintain high standards in that regard and a breach of Clause 9.1 was ruled.

The Panel noted its rulings and comments above but did not consider that the particular circumstances of this case were such as to warrant a breach of Clause 2 which was a sign of particular censure. No breach of Clause 2 was ruled.

**Complaint received** **26 March 2019**

**Case completed** **2 October 2019**

**CASE AUTH/3177/3/19**

# COMPLAINANT v GRÜNENTHAL

## Promotional Use of LinkedIn

**A complainant, who described him/herself as a concerned UK health professional, complained about a LinkedIn post from the Grünenthal Group. The post, which had been 'liked' by a named individual, read: 'We're acquiring the global rights for Qutenza [capsaicin], a highly effective pain product which complements our existing pain portfolio and is a real alternative to the current standard of care'.**

**The complainant noted that the LinkedIn post in question would have been sent to health professionals and members of the public alike. The complainant considered that the post generally promoted with little or no company oversight.**

**The detailed response from Grünenthal is given below.**

**In the Panel's view, it was not unacceptable for companies to use LinkedIn accounts or for employees to use personal LinkedIn accounts. Whether the Code applied would take into account circumstances including: the content, direct or indirect reference to a product, how the information was disseminated on LinkedIn, the company's role in relation to the availability of the content and whether such activity was instructed or encouraged by the company. If activity was found to be within the scope of the Code, the company would be held responsible.**

**The Panel noted that the LinkedIn post in question referred positively to a prescription only medicine, Qutenza, and its use in the treatment of pain. Grünenthal submitted that the LinkedIn post was placed by Grünenthal GmbH, based in Germany, without the UK company's knowledge and outside of its control; the individual who had 'liked' the LinkedIn post was employed in the UK organisation. The Panel considered that on the balance of probabilities the employee's 'like' had been disseminated to his/her connections on LinkedIn and that such dissemination was the subject of complaint.**

**The Panel noted Grünenthal's submission that the employee's LinkedIn network included individuals who were not health professionals or other relevant decision makers. The Panel considered that the proactive dissemination of the post to those who were not health professionals or other relevant decision makers constituted promotion of a prescription only medicine to the public. The Panel also considered that the positive statements in the post could have, on the balance of probabilities, encouraged members of the public to ask their health professional to prescribe Qutenza. Breaches of the Code were ruled as acknowledged by Grünenthal.**

**The Panel noted that the Code required a side-effect reporting statement to be included on material which related to a medicine and which was intended for patients taking that medicine. The Panel did not consider that the disseminated post was intended for patients taking Qutenza and therefore ruled no breach in that regard.**

**The Panel considered that the Grünenthal employee had disseminated promotional information about Qutenza to health professionals and/or other relevant decision makers within his/her network without prescribing information and other obligatory information. Breaches of the Code were ruled. The material should have been certified for such use. A breach of the Code was ruled as acknowledged by Grünenthal.**

**The Code stated that promotional material about prescription only medicines directed to a UK audience which was provided on the Internet must comply with all relevant requirements of the Code. The Panel noted its ruling of breaches of the Code and consequently ruled a further breach of the Code as acknowledged by Grünenthal.**

**The Panel noted that the Code stated that the telephone, text messages, email and the like must not be used for promotional purposes, except with the prior permission of the recipient. The Panel understood that when individuals joined LinkedIn they did so on the understanding that they might receive notification updates from people in their network. Such updates might include activities such as a connection's 'likes'. The Panel did not have before it the relevant LinkedIn terms and conditions accepted by the complainant or the employee's connections but considered it unlikely that those terms and conditions would have included an agreement to receive promotional material from pharmaceutical companies. In the Panel's view, on the balance of probabilities, the employee in question had not obtained prior permission from his/her connections on LinkedIn before disseminating promotional information. The Panel therefore ruled a breach of the Code as acknowledged by Grünenthal.**

**In the Panel's view, rulings of breaches of the Code did not in itself mean that a company had not met the training requirements set out in the Code. The Panel noted Grünenthal's submission that following the publication of Case AUTH/3038/4/18, it understood that 'liking' a post could be seen as a positive endorsement when done by an employee of a UK company and might come into the scope of the Code. The Panel noted Grünenthal's submission that whilst the complaint was received after the publication of Case AUTH/3038/4/18, the activity in question had occurred some time**

**before and that prior to receipt of the complaint the company had notified all staff on the learnings from Case AUTH/3038/4/18 but did not ask them to retrospectively assess their historic activity which remained on the Internet. The Panel noted the training the named employee had completed prior to his/her 'liking' the post in question and that the company had some UK social media guidance for employees at the time of the activity in question which was being updated following Case AUTH/3038/4/18. The Panel considered that the complainant had not shown, on the balance of probabilities, that a breach of the Code had occurred in this regard and no breach was ruled.**

**The Panel noted its comments and rulings above and considered that high standards had not been maintained and ruled a breach of the Code.**

A complainant, who described him/herself as a concerned UK health professional, complained about a LinkedIn post from the Grünenthal Group. A screenshot of the post was provided which showed that the post had been 'liked' by a named individual. The post read: 'We're acquiring the global rights for Qutenza [capsaicin], a highly effective pain product which complements our existing pain portfolio and is a real alternative to the current standard of care. Read more: [link provided].'

**COMPLAINT**

The complainant referred to companies using LinkedIn to promote products and noted that the LinkedIn post in question would have been sent to many people – health professionals and members of the public. The complainant considered that the post generally promoted with little or no company oversight and that Clauses 4.1, 4.2, 4.3, 4.4, 4.9, 7.10, 9.1, 9.9, 14.1, 14.6, 16.1, 26.1, 26.2, 26.3 and 28.1 should be considered. The complainant stated that because online platforms were new and exciting meant that more care should be taken, not less.

Grünenthal was asked to respond to the clauses cited by the complainant in relation to the requirements of the 2016 Code.

**RESPONSE**

Grünenthal explained that the LinkedIn post in question was placed by the global communications department of Grünenthal GmbH, in Germany, on 5 November 2018, without the UK company's knowledge and outside of its control. The post was intended to link to a press release hosted on the global website about the news that Grünenthal had recently acquired the global commercial rights to Qutenza. Grünenthal further explained that a current UK employee [named in the complainant's screen shot] 'liked' the post when it appeared within his/her LinkedIn feed. The employee did not actively seek the post, nor was he/she a targeted recipient, it seemed that it appeared in his/her feed as he/she had 'followed' the Grünenthal Group organisation within the tool.

Following the publication of Case AUTH/3038/4/18 in February 2019, Grünenthal understood that 'liking' a post (in addition to commenting on or sharing it), could be seen to be a positive endorsement when done by an employee of a UK company and could come into the scope of the Code. Case AUTH/3038/4/18 was a landmark case and on 28 February, Grünenthal notified all staff on the learnings from it. Additionally, a head office meeting on 19 March included a broad discussion with employees of the learnings. In addition, it was announced at that meeting that the internal policy 'Use of digital media in the conduct of business – UK & IE' would need to be updated to incorporate the new clarity on interpretation. The presentation from the meeting (copy provided) was shared with field based Compliance Champions to use with their local regional teams rather than providing it as an attachment to a centrally distributed email.

Seven new starters to the company did not attend the meeting on 19 March and email accounts had not necessarily been created for most of them on 29 February 2019, therefore a compliance member of staff specifically addressed this topic during the face-to-face new starter compliance training session on 25 March 2019. Grünenthal was thus confident that all current UK employees knew about the learnings from Case AUTH/3038/4/18.

In hindsight, and considered only upon receipt of this complaint, Grünenthal did not ask staff to retrospectively assess their historic activity on LinkedIn which remained current on the Internet, to edit anything that would fall out of scope of the new directions given by the company. Grünenthal had subsequently responded to this and an additional specific communication regarding historical activity on social media was sent to all staff on 1 April.

Grünenthal in the UK understood that linking the name of a product, with any of its indications, was likely to make a communication promotional (notwithstanding the exemptions detailed in Clause 1.2). The post in question was intended to provide a link to a company press release, however, the use of certain words in the LinkedIn post were likely to be deemed to promote Qutenza. In light of the information from Case AUTH/3038/4/18, the fact that a UK employee had 'liked' the post would be seen to be a positive endorsement of a promotional message to those in that employee's network, which included individuals who were not health professionals or other relevant decision makers.

Although Grünenthal had no confirmation that a member of the public had seen the post as a result of the UK employee 'liking' it, the company accepted that, whilst absolutely innocent in intent, there had been inadvertent and unintended breaches of Clauses 26.1, 26.2, 28.1 and 9.9. In turn, Grünenthal submitted that it must accept that there was a failure to certify the material as per Clause 14.1 as alleged.

With regard to Clause 4, Grünenthal stated that when it engaged in the development and approval of promotional material in the UK, it adhered fully to the Code, including the provision of prescribing information and other obligatory information. The LinkedIn post at issue was not developed by, nor with the authority of the UK company, and therefore

was not subject to local rigor. It was not developed as a promotional item according to local standards, it was only based on the technicality that a UK employee 'liked' the post, that it was deemed to be promotional. As such, the requirements of Clauses 4.1, 4.2, 4.3, 4.4 and 4.5 were not considered.

The LinkedIn post was not drafted to be a promotional communication, and the standards applicable in Germany did not interpret linking a product name and an indication likely to make a communication promotional, as it did in the UK.

The UK employee did not intend to 'like' the post in order to promote the medicine. There was no guidance available when the UK employee 'liked' the post to indicate that this could be interpreted as so, therefore Grünenthal disagreed that it had set out not to provide prescribing and other obligatory information required when drawing up promotional material.

Similar to the explanation above, Grünenthal did not consider that it had drawn up promotional material that exaggerated the properties of Qutenza. Although the company would not choose the wording in question for UK material, no superlatives were used and no statement of special merit was contained therein. Grünenthal therefore refuted the alleged breach of Clause 7.10.

Grünenthal acknowledged that there had been a failure to certify material, as per the requirements of Clause 14.1, but considered that the allegation of a breach of Clause 14.6 with regard to the preservation of certificates was somewhat over-reaching. Under licence, Grünenthal used two well-established electronic approval tools, within which the certificates of all material requiring certification, whether promotional or non-promotional, were stored and easily accessible. There was no issue in Grünenthal's preservation of such documents, therefore, in its view, consideration of Clause 14.6 was out of scope with regard to the complaint, and the company denied any breach of that clause.

Grünenthal considered that as the LinkedIn post was not material intended for patients taking the medicine, Clause 26.3 was not applicable.

With regard to training obligations (Clause 16.1), and internal high standards related to commitment and adherence to the requirements of the Code, Grünenthal stated that it had two local quality documents related to interactions with social media 'Use of digital media in the conduct of business – UK & IE' and 'Acceptable use of email, Internet and social media UK & Ireland' (copies provided). In addition, there was a Global Code of Conduct that briefly referred to the use of social media and the Global Promotion & Marketing Policy.

There was specific discussion on the use of digital media by employees during face-to-face new starter compliance training with all new staff and staff who returned to work following an absence of six months or longer.

With specific reference to the UK employee who 'liked' the LinkedIn post, Grünenthal provided details of his/her training record. The employee had been trained on the use of social media and the Grünenthal Global Code of Conduct.

Grünenthal thus considered that its employee had been trained in line with expectations outlined in the Code, and as noted earlier, the company continued to demonstrate ongoing high standards in its immediate internal communications about emerging learnings on application and interpretation of the Code. Whilst learnings from Case AUTH/3038/4/18 would be incorporated in an update to the 'Use of digital media in the conduct of business – UK & IE' policy, this had not yet been actioned. The case report was published on 26 February 2019, internally emailed on 28 February 2019, and in March Grünenthal had prioritised the submission of its disclosure of transfers of value. Grünenthal wanted to thoroughly review the full policy, rather than just updating one small piece. To do this properly required time and due consideration, and the company expected to have an update published by the end of April. Grünenthal submitted that this was discussed and planned before the company was notified of this complaint.

Grünenthal questioned the motivation behind this complaint. The company was fully committed to the principles of self-regulation, and it was aware that there was a genuine learning for it in terms of asking employees to retrospectively assess historical activity on LinkedIn whilst providing internal clarification on the rulings made in Case AUTH/3038/4/18, but it was entirely evident that the UK employee did not intend to promote a prescription only medicine to the public through 'liking' the LinkedIn post in question. Given what happened, Grünenthal submitted that it was right that it should be made aware of the matter, whether directly from an external party, or through the formal PMCPA complaints procedure. However, if the purpose of the complaint was to elicit redress, the issue could have been presented factually to the PMCPA for its consideration of applicable clauses, rather than the complainant listing fourteen clauses that he/she thought should be considered. Grünenthal hoped that in its response above, the Panel considered the allegations of so many additional clause breaches was excessive, unsubstantiated, and questionable in motive.

The screenshot provided by the complainant indicated that he/she viewed the LinkedIn post 3 weeks after it was published (circulated the week commencing 26 November 2018) but did not complain until 28 March 2019. Grünenthal queried why there was such a prolonged delay.

**PANEL RULING**

The Panel noted that LinkedIn was a business and employment-orientated network and was primarily, although not exclusively, associated with an individual's professional heritage and current employment and interests. In the pharmaceutical industry, the Panel noted that an individual's network might, albeit not exclusively, be directly or indirectly associated with the healthcare industry. In the Panel's view, it was of course not unacceptable

for companies to use LinkedIn accounts or for employees to use personal LinkedIn accounts. The Code would not automatically apply to all activity on an account; whether the Code applied would be determined on a case-by case basis taking into account all the circumstances including: the content, any direct or indirect reference to a product, how the information was disseminated on LinkedIn, the company's role in relation to the availability of the content and whether such activity was instructed or encouraged by the company. If activity was found to be within the scope of the Code, the company would be held responsible.

The Panel noted that the LinkedIn post in question referred to a prescription only medicine, Qutenza, and its use in the treatment of pain. The post included positive statements including that Qutenza was 'highly effective' and an 'alternative to the current standard of care' and invited the reader to 'Read more' by weblink. The Panel noted Grünenthal's submission that the post was intended to link to a press release hosted on the global Grünenthal website about the news that Grünenthal had recently acquired the global commercial rights to Qutenza. Grünenthal did not provide a copy of this press release. Grünenthal submitted that the LinkedIn post was placed by Grünenthal GmbH, based in Germany, without the UK company's knowledge and outside of its control.

The Panel noted Grünenthal's submission that an employee within the UK organisation, named in the complainant's screenshot, 'liked' the post in question when it appeared within his/her LinkedIn feed. The Panel noted that an individual could endorse a post on LinkedIn in a number of ways including 'sharing', 'liking' or 'commenting'. The Panel understood that if an individual 'liked' a post it increased the likelihood that the post would appear in his/her connections' LinkedIn feeds. The Panel considered that on the balance of probabilities the employee's 'like' had been disseminated to his/her connections on LinkedIn and that such dissemination was the subject of complaint.

The Panel noted Grünenthal's submission that the employee's network included individuals who were not health professionals or other relevant decision makers. The Panel considered that the proactive dissemination of the post, which contained statements about Qutenza, to those who were not health professionals or other relevant decision makers constituted promotion of a prescription only medicine to the public. A breach of Clause 26.1 was ruled as acknowledged by Grünenthal. Furthermore, the Panel considered that the positive statements in the post that Qutenza was 'highly effective' and an 'alternative to the current standard of care' could, on the balance of probabilities, have encouraged members of the public to ask their health professional to prescribe Qutenza. A breach of Clause 26.2 was ruled as acknowledged by Grünenthal.

The Panel noted that Clause 26.3 required a side-effect reporting statement to be included on material which related to a medicine and which was intended for patients taking that medicine. The Panel did not consider that the disseminated post was intended for patients taking Qutenza and therefore ruled no breach of Clause 26.3.

The Panel considered, on the balance of probabilities, that the Grünenthal employee's connections on LinkedIn would also include UK health professionals or other relevant decision makers and therefore that the employee had disseminated promotional information about Qutenza to health professionals and/or other relevant decision makers within his/her network without prescribing information, the non-proprietary name adjacent to the brand name at its first appearance, or the adverse event reporting statement as required by the Code. Breaches of Clauses 4.1, 4.3 and 4.9 were ruled. The material should have been certified for such use. A breach of Clause 14.1 was ruled as acknowledged by Grünenthal.

The complainant raised Clauses 4.4 and 14.6. The Panel considered that these allegations were covered by the Panel's rulings of breaches of Clauses 4.1 and 14.1 respectively.

The Panel noted that Clause 28.1 stated that promotional material about prescription only medicines directed to a UK audience which is provided on the Internet must comply with all relevant requirements of the Code. The Panel noted its ruling of breaches of Clauses 4.1, 4.3, 4.9 and 14.1 above. The Panel consequently ruled a breach of Clause 28.1 as acknowledged by Grünenthal.

The Panel noted that the complainant had raised Clause 7.10 but considered that he/she had not stated why in his/her view the post in question was in breach of this clause or provided any evidence in this regard. It was not for the Panel to infer such matters and the complainant bore the burden of proof. The Panel therefore ruled no breach of Clause 7.10.

The Panel noted that Clause 9.9 stated that the telephone, text messages, email and the like must not be used for promotional purposes, except with the prior permission of the recipient. The Panel understood that when individuals joined LinkedIn they did so on the understanding that they might receive notification updates from people in their network. Such updates might include activities such as a connection's 'likes'. The Panel did not have before it the relevant LinkedIn terms and conditions accepted by the complainant or the employee's connections. The Panel considered that it was unlikely that such terms and conditions would have included an agreement to receive promotional material from pharmaceutical companies. In the Panel's view, on the balance of probabilities, the employee in question had not obtained prior permission from his/her connections on LinkedIn prior to disseminating promotional information about Qutenza. The Panel therefore ruled a breach of Clause 9.9 as acknowledged by Grünenthal.

The Panel was aware that the types of activity performed by the named employee on LinkedIn was not uncommon across the industry. In the Panel's

view, employees might feel inclined to endorse articles emanating from their company's corporate social media posts and depending on the content such activity might fall within the scope of the Code; companies therefore needed to issue specific and unambiguous guidance on personal and business use of social media. This was particularly important if UK employees were likely to follow the social media accounts of overseas affiliates which might have Codes, laws and regulations that differed to the UK. It was important that companies regularly reviewed such guidance.

In the Panel's view, rulings of breaches of the Code did not in itself mean that a company had not met the training requirements set out in Clause 16.1. Grünenthal submitted that following the publication of Case AUTH/3038/4/18, it subsequently understood that 'liking' a post could be seen to be a positive endorsement of the post when done by an employee of a UK company and might come into the scope of the Code. The Panel noted Grünenthal's submission that whilst the complaint was received after the publication of Case AUTH/3038/4/18, the activity in question had occurred some time before and that prior to receipt of the complaint the company had notified all staff on the learnings from Case AUTH/3038/4/18 but did not ask its staff to retrospectively assess their historic activity which remained on the Internet. The Panel noted the training the named employee had completed prior to his/her 'liking' of the post in question which included 'Acceptable use of email, Internet and social media UK & Ireland' and 'Use of digital media in the conduct of business – UK & IE'. The Panel noted that the company had some UK social media guidance for employees at the time of the activity in question and that this was being updated following Case AUTH/3038/4/18. The Panel considered that the complainant had not shown, on the balance of probabilities, that a breach of Clause 16.1 had occurred, and no breach was ruled.

The Panel noted its comments and rulings above and considered that high standards had not been maintained and ruled a breach of Clause 9.1.

**Complaint received** **28 March 2019**

**Case completed** **2 October 2019**

**CASE AUTH/3180/4/19**

# RESPIRATORY NURSE v ASTRAZENECA

## Material on a personal social media account

**A respiratory nurse complained about Facebook/ Instagram posts by an AstraZeneca UK sales manager. The posts referred to a named nurse who was a key opinion leader. The complainant stated that he/she attended many respiratory meetings locally and nationally and it had recently been brought to his/her attention by a colleague that a named respiratory influencer and educational nurse lead (nurse A) had posted on Facebook/Instagram a picture of his/her partner dressed up to go to an AstraZeneca sales manager's party. Nurse A also tagged the named sales manager in his/her post.**

**The complainant stated that the sales manager had also tagged nurse A in his/her pictures. The sales manager also had AstraZeneca staff at his/her party who had also been tagged and other representatives from various pharmaceutical companies. Furthermore, the sales manager had posted a picture of nurse A in February 2019 commenting about his/her long-standing friendship with him/ her. The sales manager also had many other health professionals on his/her Facebook/Instagram who might also perceive, like the complainant had, a serious breach of ethical standards and inducement to prescribe AstraZeneca medicines. The complainant submitted that companies like AstraZeneca should be responsible for the actions of their representatives and should provide sufficient training on the use of social media. The complainant queried whether Facebook/Instagram posts such as those at issue implied to members of the public and health professionals that it was acceptable for sales managers to have relationships, other than business relationships, with respiratory leaders such as nurse A. The complainant questioned how he/she could possibly now believe that nurse A talked in an unbiased and neutral manner.**

**The complainant queried whether this raised issues such as bribery and endorsement to prescribe AstraZeneca medicines. The complainant further queried what issues/concerns this raised with the public and their perception when they saw such posts. The complainant referred to frustration in terms of understanding the relationships key influencers had with representatives which should not be publicised on social media. The complainant noted that this was a manager who clearly identified him/herself as working for the pharmaceutical industry on Facebook/Instagram and who should be leading by example; if this was not addressed it would cause a norm which others might follow.**

**The detailed response from AstraZeneca is given below.**

**The Panel noted AstraZeneca's concern that the complaint was based on the existence of a private relationship but did not accept as stated by AstraZeneca that adjudicating upon it would, *inter alia*, 'make it almost impossible for members of either [health professionals or company employees] to have any kind of professional or personal relationship with each other'. In the Panel's view, whilst such relationships were of course not prohibited *per se* companies should be mindful of both the internal and external impression given by such relationships, particularly when the health professional at issue was regularly engaged by the company as a consultant or otherwise received funds from the company and/or worked in the field associated with the employee who had posted the material. Companies should give staff clear guidance on such matters.**

**In the Panel's view, it was extremely important that clear distinctions were made between business and personal arrangements and that both public and peer perception was considered in this regard.**

**AstraZeneca explained that nurse A was a health professional engaged for cross-portfolio promotional and non-promotional activities. Nurse A's current place of work fell within the geographical area covered by the sales manager's team which might call upon him/her in the normal course of their employment. The Panel noted that nurse A was also engaged as a consultant by AstraZeneca and that in many of the consultancy agreements, the sales manager had played a role, albeit that he/she did not have sole responsibility for the arrangements.**

**The post from the sales manager's personal Instagram account in February 2019 included a picture of nurse A with text beneath it describing nurse A as the sales manager's friend and details of nurse A's role as a national key opinion leader in respiratory, diabetes and cardiovascular disease, listed some positive traits he/she possessed and then stated that the sales manager loved and missed him/her and was so happy to see him/her that day. It was unclear whether the interaction referred to in this social media posting was a personal or professional meeting but the Panel noted that according to AstraZeneca the sales manager had accompanied a team member to a call on nurse A that day.**

**The Panel noted AstraZeneca's submission about the private settings on each social media account. The Panel did not consider that a private setting automatically meant that all postings from that account were outside the scope of the Code. Whether such postings came within the scope of the Code would be determined on a case by case basis taking all the circumstances into account. The Panel considered that relevant factors for consideration in such circumstances included the privacy settings, the status of the social media accounts members/**

**followers, the size of the group, the content of the post and the impression created by the postings bearing in mind any commercial and personal relationship between the relevant parties. In this particular case, it appeared that the sales manager's private social media accounts members/followers included health professionals, including nurse A. The Panel noted that the complainant was shown the post by a colleague, it was not known whether the complainant was a follower or friend of the sales manager's Instagram/Facebook account him/herself.**

**In relation to the alleged posts about the sales manager's party the Panel noted that the posts might potentially fall within the scope of the Code; the Panel, however, had not been provided with a copy of these posts by either party. The Panel noted that the burden of proof was borne by the complainant and that the parties accounts differed. The complainant did not provide a copy of the party posts referred to although a brief description was given. The Panel considered that the complainant had not established that the Facebook/Instagram posts in relation to the sales manager's party constituted a failure of the sales manager to maintain a high standard of ethical conduct and the Panel ruled no breach of the Code in that regard.**

**The Panel noted that whilst the Instagram post in question did not mention AstraZeneca, its medicines or disease awareness, the post was made by an AstraZeneca employee in a managerial role about nurse A who worked in the same geographical area that the employee worked in and within a therapy area in which AstraZeneca had a commercial interest. Further, the health professional was engaged by AstraZeneca for various activities. The post described nurse A as a key opinion leader in three specific therapeutic areas including respiratory. The Panel only had the redacted post, it did not know how the sales manager described him/herself on Instagram. The complainant stated that the sales manager had not hidden that he/she was a member of the pharmaceutical industry. In the Panel's view, given the above factors, the Instagram post, albeit on the employee's personal Instagram account with private settings came within the scope of the Code. The Panel noted its view that whilst such relationships were of course not prohibited *per se* companies should be mindful of both the internal and external impression given by social media posts in relation to such relationships. The Panel noted that there was a difference in referring to a friend, who might be a health professional within a general social media post and referring to that friend as a key opinion leader in an area in which your company had a commercial interest and in which the company employee worked. Taking all the circumstances into account and, in particular, noting the impression given, the Panel considered that the Instagram post in question constituted a failure of the sales manager to maintain a high standard of ethical conduct and a breach of the Code was ruled.**

**The Panel considered that given the relationship between nurse A and the sales manager it was critical that AstraZeneca had processes in place to ensure that the consultancy arrangements were robust and stood up to external scrutiny. The Panel noted that whilst it had some concerns about the transparency of the arrangements, the complainant had provided no evidence to show that the arrangements for the services provided by nurse A to AstraZeneca had been inappropriate, that there had not been a legitimate need for such services or that the engagement had been an inducement to prescribe, supply, administer, recommend, buy or sell any medicine. Nor had the complainant established that the nurse in question had spoken in a biased manner on behalf of AstraZeneca as a result of the relationship. No breach of the Code was ruled.**

**The sales manager had submitted annual declarations since December 2017 in which no conflict of interest had been declared as due to previous discussions with his/her line manager, the sales manager believed that a declaration of this personal relationship was not necessary. In the Panel's view, there was a clear potential conflict of interest given that the sales manager could raise or approve a service agreement with nurse A and, in addition, a perceived conflict of interest regardless of the sales manager's approval role. The Panel considered that AstraZeneca's conduct in this regard had not maintained high standards. A breach of the Code was ruled.**

A respiratory nurse complained about Facebook/Instagram posts by an AstraZeneca UK Limited sales manager. The posts referred to a named nurse who was a key opinion leader.

**COMPLAINT**

The complainant stated that he/she was a long-standing respiratory nurse who attended many respiratory meetings locally and nationally. It had recently been brought to his/her attention by a colleague that a named respiratory influencer and educational nurse lead (nurse A) had posted on Facebook/Instagram a picture of his/her partner dressed up to go to an AstraZeneca sales manager's party. Nurse A also tagged the named sales manager in his/her post.

The complainant stated that the sales manager had also tagged nurse A in his/her pictures. The sales manager also had AstraZeneca staff at his/her party who had also been tagged and other representatives from various pharmaceutical companies. Furthermore, the sales manager had posted a picture of nurse A in February 2019 commenting about his/her long-standing friendship with him/her. The sales manager also had many other health professionals on his/her Facebook/Instagram who might also perceive, like the complainant had, a serious breach of ethical standards and inducement to prescribe AstraZeneca medicines. The complainant submitted that companies like AstraZeneca should be responsible for the actions of their representatives and should provide sufficient training on the use of social media. The complainant queried whether Facebook/Instagram posts such as those at issue implied to members of the public and health professionals that it was acceptable for sales managers to have relationships, other than business relationships, with respiratory leaders such as nurse A.

The complainant stated that this now questioned the opinions of key respiratory educational leads/ speakers like nurse A who talked nationally. The complainant questioned how he/she could possibly now believe that nurse A talked in an unbiased and neutral manner.

The complainant was alarmed as to how inappropriate it was for a well-respected company such as AstraZeneca to allow for its employees to act in such an unprofessional manner. The complainant considered that this was an endorsement of AstraZeneca and others might perceive that to be too. If all pharmaceutical companies did this then where was the ethical conduct for health professionals in what was best for the patients when they attended educational talks by key influencers such as nurse A? The complainant queried whether this raised issues such as bribery and endorsement to prescribe AstraZeneca medicines. The complainant further queried what issues/concerns this raised with the public (other Facebook and Instagram members) and their perception when they saw the posts with the sales manager and nurse A and the local respiratory market and transfer of value.

The complainant referred to frustration in terms of understanding the relationships key influencers had with representatives. This should not be publicised on Facebook/Instagram and high ethical standards should be adhered to at all times. The complainant stated that his/her daily job was to provide the best possible options for his/her patients and he/ she found this highly disrespectful as a health professional.

In further correspondence the complainant stated that he/she did not have any evidence as he/she was shown the pictures/posts by a colleague who was equally as shocked as him/her. The complainant was sure the AstraZeneca staff who were also tagged as present in the pictures should be able to verify that nurse A was present among the public members and other pharmaceutical colleagues/friends who had been tagged too. The Facebook/Instagram posts demonstrated two separate events where nurse A had been tagged and written about on the sales manager's social media accounts. The sales manager clearly identified him/herself as working with AstraZeneca on his/her LinkedIn account and it was not hidden that he/she was a member of the pharmaceutical industry too on his/her Facebook and Instagram.

The way that the relationship between Nurse A and the sales manager was perceived was very important and medicines developed and produced by multi-national companies such as AstraZeneca should be based on evidence; posts on social media somewhat distorted that. It seemed as though there were 'clicks' within the pharmaceutical industry between representatives and key influencers such as nurse A which showed an image which was not in line with the Code.

The complainant stated that having read the Code he/she submitted that there was a clear breach of ethical conduct on behalf of AstraZeneca. What was most disturbing was that this was a manager who should be leading by example and why was this behaviour encouraged as clearly there were AstraZeneca staff at the party too. What example did this set to the company and other representatives too? The complainant stated that if this was not addressed it would cause a norm which others might follow.

When writing to AstraZeneca, the Authority asked it to consider the requirements of Clauses 9.1 and 15.2 of the Code.

**RESPONSE**

AstraZeneca noted that the complaint concerned the use of personal social media accounts by one of its sales managers, nurse A and nurse A's partner. During its investigation, AstraZeneca had noted that nurse A's partner was not a health professional and that the sales manager in question had no direct relationship with nurse A's partner: the scope of the response below was thus limited to interactions with nurse A.

AstraZeneca stated that it took its obligations under the Code very seriously and had investigated the points raised by the complainant. The company understood the importance of its responsibilities regarding the use of company owned social media channels and mention of company information on personal social medial accounts. As such, AstraZeneca had a Global Standard – Employee Use of Social Media (copy provided), to guide employees with respect to mention of AstraZeneca diseases and medicines on social media platforms.

AstraZeneca noted that the privacy settings for the sales manager's social media accounts were set to private: this meant that these accounts were not open to the public. This had two important implications for this case. Firstly, whilst the AstraZeneca Global Standard – Employee Use of Social Media provided the governance framework for social media activity related to AstraZeneca, its products and disease education/awareness, it did not (and nor would it be appropriate to) govern personal social media activity beyond this remit. Secondly, the colleague who brought these posts to the complainant's attention must have also been a member of the sales manager's private group.

The professional relationship between the sales manager and nurse A started when the sales manager was a representative. Their personal relationship developed subsequently as a result of mutual interests which were not associated with the pharmaceutical industry, AstraZeneca or medicines. The sales manager confirmed that nurse A and his/ her partner were invited to his/her party but were not able to attend.

AstraZeneca provided a copy of the Instagram message, referred to by the complainant, which was posted in February 2019 from the sales manager's private account. With respect to the messages that had been posted by nurse A, AstraZeneca would need to gain his/her permission for use of

screenshots that existed on his/her personal page or images of them on the sales manager's personal page and so these had not been provided.

AstraZeneca explained that nurse A was a health professional who AstraZeneca engaged for cross-portfolio promotional and non-promotional activities.

AstraZeneca stated that as nurse A's current place of work fell within the geographical area covered by the sales manager's team, they might call upon him/her in the normal course of their employment. Sales managers in AstraZeneca did not actively plan to see specific health professionals as part of the normal course of their employment. However, they were required to accompany team members when they called upon health professionals for coaching purposes. The last interaction the sales manager at issue had with nurse A was in February 2019 when he/she accompanied a team member for coaching purposes. AstraZeneca was confident that the interactions between nurse A and both AstraZeneca and the sales manager at issue were not excessive or inappropriate.

In the past 27 months (ie between 1 January 2016 - 5 April 2019), several meetings were recorded between nurse A and a number of AstraZeneca employees across respiratory, diabetes and cardiovascular teams. No calls/group meetings had been recorded between nurse A and the sales manager in this time period. Since becoming a sales manager, a number of calls/group meetings had taken place between nurse A and members of the sales manager's team. Since 2016, nurse A had interactions with AstraZeneca employees at a number of exhibition meetings. No interaction was associated with the sales manager in question. Details regarding the number of meetings were provided.

AstraZeneca provided a list of all the contracts it had with nurse A between 1 January 2016 and 5 April 2019. Some of the historical data was outstanding and the company was in the process of retrieving it.

AstraZeneca noted that in the last 27 months, several contracts between AstraZeneca and nurse A were raised and approved. Based on the available information, all of these contracts were related to speaker meetings and the sales manager had raised around a quarter of these which were approved by a line manager, and as a line manager the sales manager approved a small number which were raised by his/her team. Details regarding the number of contracts was provided and for context AstraZeneca provided the number of contracts the sales manager in question had raised for other health professionals in a similar time period.

AstraZeneca considered that the contracts raised by the company for nurse A were fair and appropriate. There was no evidence to suggest undue influence or unethical behaviour between nurse A and either AstraZeneca or the sales manager.

AstraZeneca stated that it required employees to inform the business of any actual or potential conflicts of interest so that mitigating actions could be put in place if deemed necessary.

The sales manager's line manager at the time confirmed that he/she had told him/her of the personal relationship with nurse A and of the social media connectivity. The line manager did not consider the relationship warranted any further declaration or remediation.

In December 2017, AstraZeneca introduced the requirement to submit annual declarations of conflict of interest. The sales manager had submitted annual declarations in which no conflict of interest had been declared. In line with previous discussions between the sales manager and his/her line manager, the sales manager believed that a declaration of this personal relationship was not necessary. AstraZeneca was in the process of coaching the sales manager and his/her current line manager to declare this personal relationship as a potential conflict of interest and confirm on an annual basis whether remediation was required.

In conclusion, AstraZeneca submitted that high standards had been maintained by the company and the sales manager at all times. The company denied any breach of Clauses 9.1 and 15.2 of the Code.

AstraZeneca added that it was concerned that this complaint was, in essence, based merely on the existence of a private relationship between a health professional and an employee of a pharmaceutical company and that it created a precedent which could lead to the PMCPA being compelled to investigate any complaint which alleged some non-specified wrongdoing based purely on the existence of such relationships. This could result in the self-regulatory complaints process becoming a vehicle for arbitrating private disputes and potentially defamatory allegations involving health professionals and members of the pharmaceutical industry. This would place an unmerited and unconscionable burden on both the industry and the medical profession and make it almost impossible for members of either to have any kind of professional or personal relationship with each other.

AstraZeneca provided information regarding the list of contracts between AstraZeneca and nurse A, that it acknowledged were outstanding with its initial response due to a change in systems. AstraZeneca provided an updated list of contracts. Over a third (not a quarter as previously indicated) of the contracts raised between AstraZeneca and nurse A were raised by the sales manager over the last 27 months.

AstraZeneca submitted that the additional information did not change AstraZeneca's original response; it still considered that the contracts raised by AstraZeneca for nurse A were fair and appropriate. There was no evidence to suggest undue influence or unethical behaviour between nurse A and both AstraZeneca and the sales manager in question. AstraZeneca therefore refuted the allegation of breaches of Clauses 15.2 and 9.1.

**PANEL RULING**

The Panel noted the complainant's concerns regarding the impression created by publicising the personal relationship between an AstraZeneca sales manager and nurse A on social media.

The Panel noted that the complainant had the burden of proving his/her complaint on the balance of probabilities. A judgement had to be made on the available evidence. The Panel noted that whilst the complainant stated that he/she did not have any evidence as he/she was shown the social media pictures/posts by a colleague he/she had described the material at issue.

The Panel noted AstraZeneca's concern that the complaint was based on the existence of a private relationship but did not accept as stated by AstraZeneca that adjudicating upon it would, *inter alia*, 'make it almost impossible for members of either [health professionals or company employees] to have any kind of professional or personal relationship with each other'. In the Panel's view, whilst such relationships were of course not prohibited *per se* companies should be mindful of both the internal and external impression given by such relationships, particularly when the health professional at issue was regularly engaged by the company as a consultant or otherwise received funds from the company and/or worked in the field associated with the employee who had posted the material. Companies should give staff clear guidance on such matters.

In the Panel's view, it was extremely important that clear distinctions were made between business and personal arrangements and that both public and peer perception was considered in this regard.

The Panel noted AstraZeneca's submission that the professional relationship between the sales manager and nurse A started when the sales manager was a representative and their personal relationship developed subsequently as a result of mutual interests which were not associated with the pharmaceutical industry, AstraZeneca or medicines.

AstraZeneca explained that nurse A was a health professional engaged for cross-portfolio promotional and non-promotional activities. AstraZeneca stated that nurse A's current place of work fell within the geographical area covered by the sales manager's team which might call upon him/her in the normal course of their employment. The Panel noted that according to AstraZeneca, between 1 January 2016 and 5 April 2019 no calls/group meetings had been recorded between nurse A and the employee in question and since becoming a sales manager, a number of calls/group meetings had taken place between nurse A and members of the sales manager's team. The last interaction the sales manager in question had with nurse A was in February 2019 when he/she accompanied a team member on a call with nurse A for coaching purposes. The Panel noted AstraZeneca's submission that the interactions between nurse A and both AstraZeneca and the sales manager at issue were not excessive or inappropriate.

The Panel noted that nurse A was also engaged as a consultant by AstraZeneca. The Panel noted that in many of the consultancy agreements with nurse A, the sales manager had played a role, albeit that he/she did not have sole responsibility for the arrangements. Out of several contracts raised for nurse A over the last 27 months, the sales manager had raised over a third which were approved by his/her line manager, and as a line manager the sales manager approved a small number which were raised by his/her team. The Panel noted AstraZeneca's submission that the contracts raised were fair and appropriate and there was no evidence to suggest undue influence or unethical behaviour between nurse A and either AstraZeneca or the sales manager.

With regard to the social media posts, the Panel noted that the parties' accounts differed with regard to nurse A's attendance at the sales manager's party; the complainant stated that nurse A had posted on Facebook/Instagram a picture of his/her partner dressed up to go to the named AstraZeneca sales manager's party and the sales manager had also tagged nurse A in his/her pictures from the party. According to AstraZeneca, however, the sales manager confirmed that nurse A and his/her partner were invited to his/her party but were not able to attend.

The Panel noted that the complainant referred to a second post on Instagram by the sales manager in February 2019. AstraZeneca provided a copy of a post from the sales manager's personal Instagram account which included what appeared to the Panel to be a picture of nurse A (face redacted) with text beneath it describing nurse A as the sales manager's friend. The post included details of nurse A's role as a national key opinion leader in respiratory, diabetes and cardiovascular disease, listed some positive traits he/she possessed and then stated that the sales manager loved and missed him/her and was so happy to see him/her that day. It was unclear whether the interaction referred to in this social media posting was a personal or professional meeting but the Panel noted that according to AstraZeneca the sales manager had accompanied a team member to a call on nurse A that day.

The Panel noted AstraZeneca's submission that the sales manager's social media accounts were private and further noted the company's submission that whilst the AstraZeneca Global Standard – Employee Use of Social Media document provided the governance framework for social media activity related to AstraZeneca, its products and disease education/awareness, AstraZeneca did not (and nor did it consider it would be appropriate to) govern personal social media activity beyond this remit.

The Panel noted AstraZeneca's submission about the private settings on each social media account. The Panel did not consider that a private setting automatically meant that all postings from that account were outside the scope of the Code. Whether such postings came within the scope of the Code would be determined on a case by case basis taking all the circumstances into account. The Panel

considered that relevant factors for consideration in such circumstances included the accounts privacy settings, the status of the social media accounts members/followers, the size of the group, the content of the post and the impression created by the postings bearing in mind any commercial and personal relationship between the relevant parties. In this particular case, it appeared that the sales manager's private social media accounts members/followers included health professionals, including nurse A. The Panel noted that the complainant was shown the post by a colleague, it was not known whether the complainant was a follower or friend of the sales manager's Instagram/Facebook account him/herself.

In relation to the alleged posts about the sales manager's party the Panel noted that the posts might potentially fall within the scope of the Code; the Panel, however, had not been provided with a copy of these posts by either party. The Panel noted that the burden of proof was borne by the complainant and that the parties accounts differed. The complainant did not provide a copy of the party posts referred to although a brief description was given. The Panel considered that the complainant had not established that the Facebook/Instagram posts in relation to the sales manager's party constituted a failure of the sales manager to maintain a high standard of ethical conduct and the Panel ruled no breach of Clause 15.2 in that regard.

The Panel noted that whilst the Instagram post in question did not mention AstraZeneca, its medicines or disease awareness, the post was made by an AstraZeneca employee in a managerial role about nurse A who worked in the same geographical area that the employee worked in and within a therapy area in which AstraZeneca had a commercial interest. Further, the health professional was engaged by AstraZeneca for various activities. The post described nurse A as a key opinion leader in three specific therapeutic areas including respiratory. The Panel only had the redacted post, it did not know how the sales manager described him/herself on Instagram. The complainant stated that the sales manager had not hidden that he/she was a member of the pharmaceutical industry. In the Panel's view, given the above factors, the Instagram post, albeit on the employee's personal Instagram account with private settings came within the scope of the Code. The Panel noted its view that whilst such relationships were of course not prohibited *per se* companies should be mindful of both the internal and external impression given by social media posts in relation to such relationships. The Panel noted that there was a difference in referring to a friend, who might be a health professional within a general social media post and referring to that friend as a key opinion leader in an area in which your company had a commercial interest and in which the company employee worked. Taking all the circumstances into account and, in particular, noting the impression given, the Panel considered that the Instagram post in question constituted a failure of the sales manager to maintain a high standard of ethical conduct and a breach of Clause 15.2 was ruled.

The Panel noted the complainant's statement that based on the relationship between the sales manager and nurse A as seen in the social media posts in question, he/she queried how he/she could believe that nurse A talked in an unbiased and neutral manner and whether it raised issues such as bribery and endorsement to prescribe AstraZeneca medicines.

The Panel considered that given the relationship between nurse A and the sales manager it was critical that AstraZeneca had processes in place to ensure that the consultancy arrangements were robust and stood up to external scrutiny. The Panel noted that whilst it had some concerns about the transparency of the arrangements, the complainant had provided no evidence to show that the arrangements for the services provided by nurse A to AstraZeneca had been inappropriate, that there had not been a legitimate need for such services or that the engagement had been an inducement to prescribe, supply, administer, recommend, buy or sell any medicine. Nor had the complainant established that the nurse in question had spoken in a biased manner on behalf of AstraZeneca as a result of the relationship. No breach of Clause 9.1 was ruled.

The Panel was concerned that despite AstraZeneca's submission that it required employees to inform the business of any actual or potential conflicts of interest and the sales manager informing his/her line manager of his/her personal relationship with nurse A and of the social media connection, the line manager did not consider the relationship warranted any further declaration or remediation. The Panel further noted that despite AstraZeneca introducing the requirement to submit annual declarations of conflicts of interest in December 2017, the sales manager had submitted annual declarations in which no conflict of interest had been declared as due to previous discussions with his/her line manager, the sales manager believed that a declaration of this personal relationship was not necessary. In the Panel's view, there was a clear potential conflict of interest given that the sales manager could raise or approve a service agreement with nurse A and, in addition, a perceived conflict of interest regardless of the sales manager's approval role. The Panel considered that AstraZeneca's conduct in this regard had not maintained high standards. A breach of Clause 9.1 was ruled. The Panel noted that AstraZeneca was in the process of coaching the sales manager and his/her current line manager to declare this personal relationship as a potential conflict of interest and confirm on an annual basis whether remediation was required.

**Complaint received** **4 April 2019**

**Case completed** **29 October 2019**

**CASE AUTH/3182/4/19**

# PHARMACIST v ASTELLAS

## Frequency of telephone calls by representatives

**The complaint concerned the frequency with which Astellas representatives contacted a pharmacist with regard to Betmiga (mirabegron), used in the symptomatic treatment of patients with overactive bladder syndrome.**

**Mirabegron had not been approved for use in the local publicly-funded pharmaceutical service but the pharmacist noted that he/she regularly got telephone calls from Astellas representatives asking how it could be approved. The pharmacist had not logged the times and dates of the calls, but he/she had been receiving them on a regular basis for two or more years. In the last month he/she had received possibly four such calls. The pharmacist stated that at the very least it was inconvenient and he/she personally found it intrusive and distressing.**

**The detailed response from Astellas is given below.**

**The Panel noted Astellas' submission that there had been no recorded calls in the company's customer relationship management system to anyone in the region in question, since November 2016.**

**The Panel noted, however, that three representatives had telephoned the pharmacist between January and April 2019 with queries about the local formulary in relation to mirabegron and enzalutamide. Details were provided including that representative 2 obtained the contact details from the relevant government webpage and contacted him/her as directed by that webpage. It appeared that the pharmacist stated that he/she did not talk to industry and ended the call.**

**Representative 3 had twice tried to contact the pharmacist (21 March and 3 April) to understand the process for applying for enzalutamide to be considered on the formulary and left voice messages on both occasions. The Panel noted that this was done despite the representative knowing about representative 2's interaction with the pharmacist and his/her position on speaking with industry.**

**The Panel noted that the three representatives, had telephoned the pharmacist four times between 16 January and 3 April 2019.**

**The Panel considered that if more than one representative from a company called the same health professional or other relevant decision maker, whether in relation to the same medicine or different medicines, particular care should be taken in relation to the number, timing of, and interval between calls made by those representatives to avoid inconveniencing the individual. The Panel noted Astellas' view that as it considered medicines were not promoted during the calls the interactions were not entered on the CRM system. The Panel did not consider whether the calls were promotional or non-promotional but considered that it would be helpful if such calls were documented so that companies could assess such interactions in relation to the Code.**

**The Panel noted that representative 3 had tried to contact the pharmacist twice despite knowing his/her position on speaking with industry. The Panel noted Astellas' submission that the pharmacist was the single designated point of contact on the relevant formulary government webpage which the Panel noted provided a name and contact telephone number but no email or postal address. Nonetheless and on balance, the Panel considered that the pharmacist's wishes were not observed by representative 3 and a breach of the Code was ruled as acknowledged by Astellas. The Panel considered that representative 3 had failed to maintain a high standard of ethical conduct in this regard and a further breach of the Code was ruled as acknowledged by Astellas.**

**The Panel noted Astellas' submission that, *inter alia*, sales staff received additional training on the Code in 2017 and 2018, which specifically covered the requirements of the Code to observe arrangements in place at any particular establishment and to not cause inconvenience. A training presentation titled 'How should a representative behave?' stated, *inter alia*, that the timing and duration of calls must not cause inconvenience, that representatives must know and adhere to any local policies in place, the company's definition of a call vs a contact, and that call frequency must be no more than three per health professional per year.**

**The Panel noted its comments above and considered that it had no evidence before it that the representatives' briefing materials advocated any course of action which would likely lead to a breach of the Code in relation to calls and contacts with health professionals and other relevant decision makers, and observing the wishes of individuals and the arrangements in force in any particular establishment. The Panel therefore ruled no breach of the Code.**

**Noting its ruling of no breach of the Code above and in particular noting the content of the relevant government webpage the Panel did not consider that Astellas had failed to maintain high standards and so it ruled no breach of the Code.**

The complaint concerned the frequency with which a pharmacist had been contacted by Astellas representatives with regard to Betmiga (mirabegron), used in the symptomatic treatment of patients with overactive bladder syndrome.

**COMPLAINT**

Part of the pharmacist's job was to manage the introduction of new medicines for the state-funded pharmaceutical service. The region in question was a self-governing jurisdiction which ran its own health service, which was similar to the NHS. However, it was not required to provide funding for medicines approved via the National Institute for health and Care Excellence (NICE) technology assessments.

Mirabegron had not been approved for use in the local publicly-funded pharmaceutical service but the pharmacist noted that he/she regularly got telephone calls from Astellas representatives asking how it could be approved.

When the pharmacist first answered those calls he/she would have explained that he/she did not see people from the industry due to a very heavy workload and that companies could not request the local approval of a medicine. The pharmacist had not logged the times and dates of the calls, but he/she had been receiving them on a regular basis for two or more years. In the last month he/she had received possibly four telephone calls from representatives. The representatives had sometimes stated that a particular colleague had asked them to contact him/her. The calls were described as inconvenient, intrusive and distressing.

When writing to Astellas, the Authority asked it to consider the requirements of Clauses 9.1, 15.2, 15.4 and 15.9 of the 2016 Code.

**RESPONSE**

Astellas explained that the company consisted of three separate business units - oncology, urology and specialist brands. Each business unit had its own marketing team, field-based representatives, sales managers and a shared market access team. Each business unit worked independently and shared a common customer relationship management (CRM) system to record calls and contacts.

The CRM system showed no current account plans for any business unit for the relevant region as it had not been identified as a priority for any part of the business. However, there was limited activity by Astellas on this account between 2012 and November 2016, with no activity such as calls or contacts made on the pharmacist. There had been no recorded activity in the form of calls on anyone in this account, since November 2016. The only recent activity recorded for individuals other than the pharmacist was in regard to 'contacts', where individuals had attended meetings or congress supported by Astellas.

**Activity of the urology business unit**

In January 2019, the representative (representative 1) who covered the region in question, received sales data for November 2018 that indicated a number of prescriptions for mirabegron had been written. He/she knew that the local formulary was being updated and wondered whether mirabegron had now been included. He/she checked the relevant government website but could not see mirabegron on the list so, as directed by instructions on the website, he/she telephoned to enquire. In the telephone conversation which took place in January 2019, representative 1 introduced him/herself and asked whether mirabegron had been added to the formulary. The pharmacist asked how the representative had obtained his/her contact details and the representative explained he/she had followed the directions on the website. The pharmacist stated that the website details were not intended for people outside the region; representative 1 apologised and asked how he/she should contact the individual who replied, 'You don't'. Representative 1 then asked who he/she should contact, to which the pharmacist responded that representative 1 should 'Google it'. Representative 1 then thanked the pharmacist for his/her time and ended the telephone call and made no further contact. The pharmacist never stated that he/she did not engage directly with representatives or direct representative 1 to someone else who might be able to respond to his/her enquiry. As mirabegron was not promoted during the call and the conversation was purely an investigatory telephone discussion to understand process, Astellas submitted that there was no requirement to record the interaction in the CRM system.

**Activity of the oncology business unit**

On 26-27 November 2018, three members of the oncology business unit attended the British Association of Urological Nurses (BAUN) meeting. At this meeting, an oncology nurse from the region approached the stand to discuss another Astellas medicine, enzalutamide (Xtandi), stating that it was not on the formulary, he/she did not know why and that it might be beneficial to patients if it was added. One of the members of the oncology business unit present at BAUN (representative 2) then had a follow-on conversation with the nurse in January 2019 during which the latter recommended that the representative contact the pharmacy team and referred to the pharmacist.

Representative 2 obtained the contact details via the government website referred to above and, seeing the instruction on the website, telephoned on 21 January 2019. Representative 2 introduced him/herself and referred to the oncology nurse by name to which the pharmacist responded, 'I don't talk to Industry' and put down the telephone. No promotion took place during this interaction and thus the call was not recorded in the CRM system. Representative 2 had no further contact with the pharmacist.

Subsequently, in March 2019, representative 2 discussed this interaction with representative 3. Representative 3 had previous experience of working with the region and had met the pharmacist on one occasion over 10 years ago. Representative 3 telephoned on 21 March 2019 in order to understand the process for applying for a medicine to be considered for the formulary; he/she left a short, polite voice message introducing him/herself. As he/

she did not hear back, representative 3 made one follow-up call on 3 April 2019, again leaving a short, polite voice message on the answerphone stating that he/she wished to understand how enzalutamide might be submitted to the formulary; the message also stated that if the pharmacist preferred to speak with a company medical advisor instead of the representative then the representative could facilitate this. No products were promoted in either message and no further contact was made. Again, these telephone messages were not recorded in the CRM system.

**Clause 15.4**

Astellas submitted that it did not consider that the actions of representatives 1 and 2 were contrary to the requirements of Clause 15.4. Each representative only contacted the pharmacist once and when, as a result of these interactions, they knew his/her position on speaking to the industry they did not contact him/her again.

In relation to representative 3, he/she was in a difficult position in that the pharmacist appeared to be the only person who could provide information on how medicines could be placed on the local formulary.

However, representative 3 attempted to contact the pharmacist despite knowing that he/she had told representative 2 that he/she did not 'talk to industry'. Thus, Astellas considered that the wishes of the individual were not observed, and despite the best of intentions, the calls made by representative 3 caused inconvenience, contrary to the requirements of Clause 15.4. Astellas therefore acknowledged a breach of that clause. Astellas apologised for the inconvenience caused and had taken steps to ensure that no further contact was made with the individual.

**Clause 15.2**

As outlined in statements from each of the three representatives, the relevant government website directed enquiries about the formulary to the pharmacist as the single designated contact, therefore it was not unreasonable for each representative to assume that that individual should be contacted in order to understand whether a medicine was on the formulary, or to understand how a medicine could be placed on it.

Representatives 1 and 2 each contacted only once and did not try to do so again once his/her position in relation to the industry was indicated. With this in mind, Astellas did not consider that either representative had failed to maintain high standards and it thus denied any breach of the Code in that regard.

Astellas submitted that representative 3 did not deliberately try to be obtrusive or cause inconvenience. However, as noted above he/she tried to contact the pharmacist despite knowing that he/she did not talk to industry. In that regard, and in that exceptional circumstance, Astellas considered that representative 3 had failed to maintain high standards, in breach of Clause 15.2.

**Clause 15.9**

Astellas stated that as the region was not a priority for any of the business units, there was no briefing or instruction to staff specifically on the local arrangements.

Astellas trained all new and existing staff on the importance of high standards of the Code including Clause 15. Ethics and Compliance standards were also captured in job descriptions and annual objectives.

Code training was provided as part of the initial training course and Code updates via the company learning management system. Field-based personnel were reminded about calls and contacts standards on incentive scheme documentation and briefing materials. Further, sales staff training on the Code in 2017 and 2018 specifically covered the requirements of Clause 15.4.

Astellas did not consider that any sales force briefing documents had advocated, either directly or indirectly, any course of action, which would be likely to lead to a breach of the Code. Thus, Astellas denied a breach of Clause 15.9.

**Clause 9.1**

Given the briefing referred to above, Astellas considered that it had provided extensive briefing to its sales force in order to ensure that there was a clear and robust understanding of the requirements of the Code, including those noted in Clause 15.4 and thus it did not consider that it had failed to maintain high standards; the company denied a breach of Clause 9.1.

**PANEL RULING**

The Panel noted the allegation about the number of times the pharmacist had been contacted by Astellas representatives regarding how mirabegron could be approved for use in the local publicly-funded pharmaceutical service despite explaining when first contacted that he/she did not see people from the industry.

The Panel noted that Clause 15.4 stated that representatives must ensure that the frequency, timing and duration of calls on health professionals and other relevant decision makers in hospitals and NHS and other organisations, together with the manner in which they were made, did not cause inconvenience. The wishes of individuals on whom representatives wished to call and the arrangements in force at any particular establishment, must be observed. The supplementary information to this clause stated, *inter alia*, that the number of calls made on a doctor or other prescriber by a representative each year should not normally exceed three on average. This did not include attendance at group meetings, a visit to follow up a report of an adverse reaction, a visit which was requested or a call which was made in order to respond to a specific enquiry which might be additional to those three calls.

The Panel noted Astellas' submission that there had been no recorded calls in the company's CRM system on anyone in the region in question, including the pharmacist, since November 2016.

The Panel noted, however, that three representatives had tried to telephone the pharmacist between January and April 2019 with queries about the local formulary in relation to mirabegron and enzalutamide.

Representative 1 contacted the pharmacist once on 16 January as directed by the relevant government website to ask if mirabegron had been added to the formulary and made no further contact when informed that he/she did not engage directly with representatives of pharmaceutical companies.

Representative 2, from a different business unit, contacted the pharmacist on 21 January in relation to enzalutamide at the recommendation of an oncology nurse. The representative obtained contact details from the relevant government webpage and contacted him/her as directed by that webpage. It appeared to the Panel from Astellas' submission that the pharmacist stated that he/she did not talk to industry and put down the telephone before enzalutamide was mentioned.

The Panel noted that representative 3 had tried twice to contact the pharmacist (21 March and 3 April) to understand the process for applying for enzalutamide to be considered on the local formulary and left voice messages on both occasions. The Panel noted that this was done despite representative 3 being aware of representative 2's interaction with the pharmacist and his/her position on speaking with industry.

The Panel noted that the three representatives telephoned the pharmacist four times between 16 January and 3 April 2019 with queries about the company's medicines and the local formulary. The Panel noted Astellas' submission that the relevant government website directed enquiries about the formulary to the pharmacist as the single designated contact, therefore it was not unreasonable for the representatives to assume that the individual should be contacted in order to understand whether a medicine was on the formulary, or to understand how a medicine could be placed on the list.

The Panel considered that if more than one representative from a company called the same health professional or other relevant decision maker, whether in relation to the same medicine or different medicines, particular care should be taken in relation to the number, timing of, and interval between calls made by those representatives to avoid inconveniencing the individual. The Panel noted Astellas' view that as it considered medicines were not promoted during the calls the interactions were not entered on the CRM system. The Panel did not consider whether the calls were promotional or non-promotional but considered that it would be helpful if such calls were documented so that companies could assess such interactions in relation to Clauses 15.2 and 15.4 of the Code.

The Panel noted Astellas' submission that representatives 1 and 2 had each contacted the pharmacist once; no further contact was made once they knew the pharmacist's position on speaking to industry. The Panel noted that representative 3, however, had tried to contact the pharmacist twice despite knowing his/her position on speaking with industry. The Panel noted Astellas' submission that the individual was the single designated point of contact on the relevant government webpage which the Panel noted provided a name and contact telephone number but no email or postal address. Nonetheless and on balance the Panel considered that the pharmacist's wishes were not observed by representative 3 and a breach of Clause 15.4 was ruled as acknowledged by Astellas. The Panel considered that representative 3 had failed to maintain a high standard of ethical conduct in this regard and a breach of Clause 15.2 was ruled as acknowledged by Astellas.

The Panel noted that Clause 15.9 stated, *inter alia*, that briefing material must not advocate, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code.

The Panel noted Astellas' submission that field-based personnel were reminded about calls and contacts standards on incentive scheme documentation and briefing materials and that sales staff received additional training on the Code in 2017 and 2018, which specifically covered the requirements of Clause 15.4 to observe arrangements in place at any particular establishment and to not cause inconvenience. The Panel noted that a training presentation titled 'How should a representative behave?' stated, *inter alia*, that the timing and duration of calls must not cause inconvenience, that representatives must know and adhere to any local policies in place, the company's definition of a call versus a contact, and that call frequency must be no more than three per health professional per year.

The Panel noted its comments above and considered that it had no evidence before it that the representatives' briefing materials advocated any course of action which would likely lead to a breach of the Code in relation to calls and contacts with health professionals and other relevant decision makers, and observing the wishes of individuals and the arrangements in force in any particular establishment. The Panel therefore ruled no breach of Clause 15.9.

Noting its ruling of no breach of Clause 15.9 above and in particular noting the content of the relevant government webpage the Panel did not consider that Astellas had failed to maintain high standards in this regard and ruled no breach of Clause 9.1.

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|---|---|
| **Complaint received** | **10 April 2019** |
| **Case completed** | **2 October 2019** |

# ANONYMOUS, NON-CONTACTABLE v ALMIRALL

## Arrangements for a meeting

**An anonymous, non-contactable ex-employee complained about the arrangements for a meeting, 'Psoriasis Management of Patients Over Time – PsoMOT', organised by Almirall Spain to which UK doctors were invited to attend.**

**The complainant alleged that Almirall UK selected and invited UK doctors to attend the lavish meeting in Berlin on Friday, 26 October 2018 based on their prescribing of Almirall products.**

**The meeting was attended by Almirall UK representatives and on Friday, 26 October guests flew in for a lavish dinner. There was no educational content on that day as per the invite.**

**On Saturday, 27 October there was a number of promotional presentations on Almirall's product from various paid speakers as per the agenda. In the evening a second lavish dinner with a music band and cabaret dancers was held at a named venue.**

**On Sunday there were more presentations on the company's product and the meeting finished at noon. A three course sit down lunch was provided.**

**The detailed response from Almirall is given below.**

**The Panel noted that there was no evidence that the UK invitees were chosen on the basis of their prescribing of Almirall products. The briefing to the representatives set out the criteria and the nominations were reviewed by senior employees in marketing and medical. The Panel did not consider that the complainant had provided evidence to demonstrate on the balance of probabilities that the prescribing of Almirall products was the reason for inviting the health professionals. Thus, no breach of the Code was ruled.**

**In relation to the allegations about the hospitality, the Panel noted that the limits in the host country code would apply. The limit in the German Code was €60 per meal including VAT.**

**According to the agenda for the meeting as provided by Almirall, it started at 08.15 on Saturday, 27 October and finished at 16.30 with 30 minutes for a morning coffee break and 90 minutes for lunch. The agenda for Sunday, 28 October started at 09.00 where delegates could choose to attend two sessions of parallel workshops followed by 30 minutes conclusion and wrap up finishing the meeting at 11.30. There was no mention on the agenda of the dinners on the Friday and Saturday evenings, nor of the lunch on the Sunday. The meeting schedule provided by the complainant had more detail about the arrangements including those for the dinners on Friday and Saturday and the lunch on Sunday.**

**The various groups had dinner by country at different restaurants on the Friday evening and all the delegates had dinner together on the Saturday evening, siting in country groups.**

**The Panel noted that the cost of the meal on the Friday evening for UK delegates including drinks and taxes was within the limits of the German Code requirements as was cost of the dinner on the Saturday evening.**

**There was no agenda, presentations nor educational content provided on the Friday as alleged. The Panel considered that it was not necessarily unacceptable to offer subsistence to delegates who had arrived the day prior to the meeting. The Panel noted that a buffet lunch was offered on the Sunday. The Panel queried whether the arrangements for the lunch on the Sunday were appropriate noting that it was served 30 minutes after the end of the meeting and cost €42.35 per person including alcohol. In the Panel's view, this was on the limits of acceptability.**

**The Panel noted Almirall's submission for the arrangements for the dinner on the Saturday evening. It was held in the venue mentioned by the complainant, however, Almirall submitted that the room had been laid out very differently and there was no music or cabaret dancers contrary to the photographs provided by the complainant. The company submitted that no entertainment was provided and that the photographs provided by the complainant were from another event at the venue on a different date. The Panel did not consider that the complainant had provided evidence to demonstrate on the balance of probabilities that entertainment other than food and drink was provided.**

**The Panel considered that it was important for a company to be mindful of the impression created by its activities. Taking all the circumstances into account the Panel did not consider that the hospitality on the Friday, Saturday or Sunday was, on balance, unreasonable. The Panel ruled no breach of the Code.**

**The Panel noted its rulings and the lack of evidence. The complainant had not shown that high standards had not been maintained. The Panel ruled no breaches of the Code including no breach of Clause 2.**

An anonymous, non-contactable ex-employee complained about the arrangements for a meeting, 'Psoriasis Management of Patients Over Time – PsoMOT', organised by Almirall Spain to which UK doctors were invited to attend. Almirall marketed two medicines for the treatment of moderate to severe plaque psoriasis – Skilarence (dimethyl fumarate) and Ilumetri (tildrakizumab).

**COMPLAINT**

The complainant alleged that Almirall UK invited UK doctors to attend the lavish meeting in Berlin on Friday, 26 October 2018. Almirall UK selected and invited UK doctors to attend, based on their prescribing of Almirall products.

The meeting was attended by Almirall UK representatives and on Friday, 26 October guests flew in for a lavish dinner. There was no educational content on that day as per the invite.

On Saturday, 27 October there was a number of promotional presentations on Almirall's product from various paid speakers as per the agenda. In the evening a second lavish dinner with a music band and cabaret dancers was held at a named venue.

On Sunday there were more presentations on the company's product and the meeting finished at noon. A three course sit down lunch was provided.

The complainant provided a copy of a letter to delegates setting out the final arrangements for the forthcoming meeting; he/she also provided a number of photographs from what appeared to be an evening venue.

When writing to Almirall, the Authority asked it to consider the requirements of Clauses 2, 9.1 and 22.1 of the Code.

**RESPONSE**

Almirall explained that the 2018 PsoMOT ('PsOriasis Management of patients OverTime') meeting was organised, managed and fully funded by Almirall S.A (parent company of Almirall UK), based in Barcelona, Spain. Almirall S.A also fully funded the attendance of all the UK health professionals.

Almirall submitted that PsoMOT took place in Berlin, Germany, on 27 and 28 October 2018 and was a highly educational scientific event, where renowned dermatology experts from across Europe shared their expertise. The meeting aimed to provide an opportunity for health professionals to further enhance their knowledge and experience in the area of dermatology with the interest of improving patient outcomes.

The meeting was structured into plenary lectures followed by interactive parallel workshops so that delegates could choose part of their programme according to their educational preference and interact closely with experts, as appropriate. A copy of the agenda was provided.

One hundred and fifty-one health professionals from twelve European countries, including the UK (n=17), attended the meeting and thus it was not an event specifically aimed at UK health professionals. As it was an international meeting, it was hosted in Berlin (ie a central city hub). Six international experts spoke at the meeting; none of the speakers were from the UK. Almirall provided a table to show delegate and employee attendance by country. UK health professionals were the fourth largest group behind Germany, Spain and Italy. Across all countries, 80 Almirall staff attended the meeting.

Details of the four Almirall staff attendees from the UK were provided. Their roles were to be UK points of contact for health professionals; additionally, some of those attending would benefit from the learning at the educational meeting.

Almirall stated that the company had corporate standard operating procedures (SOPs) in place to ensure baseline procedures across the organisation world-wide. The 'Prescription only medicines promotional compliance SOP' clearly outlined the arrangements for hospitality and events which was applicable to all Almirall employees. A copy was provided.

Almirall submitted that in addition to compliance with the corporate SOPs, before any global event/ meeting arrangements were made, an event was planned and all the arrangements were reviewed and approved via the global event approval form (EAF) to ensure compliance with the EFPIA Code as well as the event originator market code (in this case the Spanish Code); and the host market code, where the event was held (in this case the German Code).

The approval form for the meeting in question was compiled by global in Almirall S.A, and reviewed and approved in Germany, and also reviewed by members of the global team of Almirall S.A, from the marketing, medical and compliance departments in Spain. A copy of the form was provided.

Finally, as the meeting was organised, managed and fully funded by the global team (Almirall S.A), including the attendance of all the UK delegates, the UK team did not need to certify the arrangements for the meeting.

As stated above, the meeting was organised, managed and fully funded by Almirall S.A. The role of Almirall UK was only to nominate appropriate delegates, who were contacted directly by global to complete registration and logistical arrangements.

To approve the meeting arrangements and facilitate the nomination process and ensure compliance with the Code, the UK marketing team compiled a comprehensive local meeting approval form and a UK sales team health professional nomination briefing. The briefing, as well as the meeting approval form were reviewed by the UK and subsequently certified. Copies of the UK certified approval form and salesforce briefing were provided together with an email to the salesforce.

The only information the representatives had was in the briefing. Any further questions from health professionals about the meeting or the agenda and content etc, were referred to the UK medical team. The reactive response for the medical team was provided.

The UK nominations briefing to the salesforce provided information on the invitation process and

clearly stated that the meeting would be suitable for consultant dermatologists, specialist registrars (final year of training), associate specialists and GPs with a special interest (working in secondary care). The health professionals had to be involved in the management of psoriasis patients, have a justifiable learning need that would be met by attending the meeting and be willing to apply this learning to benefit patients, or benefit the NHS and maintain patient care. The briefing further stated that where possible Almirall should not invite health professionals who it had supported to attend previous Almirall meetings (within the last year), unless they were absolutely the most suitable person to invite from the local healthcare. Once the nominations were received by Almirall UK, they were reviewed by employees marketing and medical.

Almirall strongly disagreed with the complainant's assertion that UK health professionals were selected based on their prescribing habits of Almirall medicines, this was clearly not the case.

Almirall UK selected the individual health professionals and the global team from Almirall S.A issued the invitations and funded the trip. The UK team helped draft some of the content of the invite to ensure a smooth transition of communication to the health professionals. The UK health professionals would initially have been told about the meeting by a representative but the official invite and meeting details would have been sent from Almirall S.A although the UK team also examined the final invitation email. Copies of relevant emails were provided.

Almirall S.A was sited in Spain. Under the Spanish Code, the expenditure on subsistence was a maximum cost per guest of €60 (including taxes) for any form of hospitality associated with meals and/or lunches. The threshold for subsistence was also €60 in Germany, and according to the UK Code the cost of a meal (including drinks) provided by way of subsistence must not exceed £75 (excluding VAT and gratuities) per person.

Almirall stated that all meals (lunches and dinners) provided during the PsoMOT meeting complied with the respective code(s). In addition, no entertainment was provided during the dinner on Saturday, 27 October or any of the lunch and/or dinners during the entire meeting. As the meeting was due to start at 08.15 on Saturday, 27 October, some delegates flew in the night before. Dinners in line with the Code(s) requirements were provided.

Due to the international nature of the meeting and the large delegate group flying in from different countries, at different times, dinners at separate locations were organised on Friday, 26 October. All the venues and subsistence thresholds were within the limits of Germany, the host country for the meeting.

10 delegates in total (UK health professionals and Almirall UK staff) attended the dinner from the UK on Friday night. Almirall provided details of the dinner menu and the final invoice for the meal.

Almirall UK stated that neither it nor global (Almirall S.A) knew of any issues with the meeting or its arrangements until the letter from the Authority in May 2019 (six months after the event). At that point the company became aware of the 'fake entertainment photos' and it was clearly very surprised and perplexed.

The UK and global team had diligently and transparently worked to provide the PMCPA with an accurate response. The matter had been investigated with full support and co-operation from relevant staff members locally as well as global colleagues, including senior management.

The photographs provided by the complainant, showing entertainment, appeared to be from the venue, where various types of events took place ranging from business events, group business dinners to personal events and social events etc. The venue could be 'dressed up' accordingly. Almirall submitted however that the complainant's photographs were not from the Almirall dinner. A basic Google search for images from the venue showed one of the alleged photographs as a thumbnail on the very first page. Clicking through this photograph led to a travel advice website where the other 'entertainment' photograph was available. Although a poor quality black and white photograph was submitted by the complainant, Almirall had found the original source and colour copies of two of the four photographs – which were feely available in the public domain. Almirall submitted that this without a doubt confirmed the false nature of the complaint and the claims made by the complainant.

A PsoMOT meeting dinner was hosted at the venue on Saturday, 29 October in order to cater for a large group (>240) of attendees. The venue was a private event, solely booked for the Almirall dinner on this date and the bar was closed during the dinner. The only subsistence provided was from the pre-agreed and approved arrangements. Copies of invoices were provided together with some photographs taken by a UK employee. The venue was an industrial looking events venue, with colourful fancy lighting. It had been used by many industries, including the pharmaceutical industry. It was selected as a venue that could easily accommodate a meal for >240 attendees.

Almirall emphasised that no entertainment was provided during the dinner on the Saturday or any of the lunches or dinners during the meeting. None of the lunches or dinners at PsoMOT were lavish and all complied with the respective code(s).

No additional hospitality was provided to the UK health professionals.

Scientific sessions were held on the Sunday morning from 09.00 to 11.30. There was no 3-course sit down lunch provided on Sunday, as alleged. Instead a buffet lunch was provided at the meeting venue, immediately after the sessions finished and before attendees' return flights in the afternoon, to ensure a proper meal before the long journeys (approximately 2-4 hours travelling time) to their countries of origin

for most of the delegates. The cost breakdown of each meal was provided which included information on the menu as well as the cost of food and beverage per person, which was €42.35 – all within the code(s) thresholds. For overall completeness Almirall provided a copy of the final invoice for the PsoMOT meeting.

Almirall stated that PsoMOT was a highly educational scientific meeting. The information covered was, objective, balanced and of scientific interest. Almirall provided information on the number of slides used in each session of the meeting and how many of those slides included the names of medicines and how many referred to Almirall's medicines (Skilarence and tildrakizumab). Almirall stated that although references were made to some of its products, these were not intended to be promotional *per se*. In line with the non-promotional style of the meeting and a focus on education and science, no product branding or brand colours were used. The overall branding was Almirall corporate.

In line with standard European medical education principles, the content of the slides was managed independently by the expert speakers. All the slides were reviewed by the global medical affairs team and final revisions with the speakers were undertaken on-site in Berlin on Friday, 26 October in a slide review meeting.

In addition, to support the strength of the highly education scientific meeting, the overall attendees' evaluation of the meeting, for those who responded was very high, with all the topics and speaker evaluations achieving more than 4 rating as a quality average (from an evaluation of 1 = very poor to 5 = very good). This was testament to the intent and purpose of the educational meeting. The speaker evaluation feedback summary was provided.

The feedback from seven different UK health professionals included comments such as:

- 'The meeting was excellent – very informative.'
- 'Many thanks, [employee name redacted] for organising such an informative and enjoyable event. Your programme was well balanced and really useful for a practicing dermatologist as myself.'
- 'Dear [employee name redacted], I wanted to thank you again for the great meeting organised and your personal support.'
- 'Thank you [employee name redacted], the meeting was very helpful and well organised.'
- 'Dear [employee name redacted]Thank you for all the organisation you had done for me to attend this meeting. It was a great meeting and was organised well.'
- 'Thank you very much. It was a really useful event. Thank you for everything.'
- 'Kindly keep me posted any further future meetings/events.'

In summary, Almirall stated that it took its commitment to, and compliance with, the Code very seriously, with this ethos applied to everything it did. The company noted that the meeting took place in October 2018 and it had taken over six months for the anonymous ex-employee to falsely report the matter and ask the PMCPA to investigate this complaint as a matter of urgency. Almirall could not help but be suspicious about the motives behind the allegations, especially combined with the false photographs. Almirall denied all alleged breached of the Code.

**PANEL RULING**

The Panel considered this case under the 2016 Code. It noted there were differences between that Code and the current Code, the 2019 Code, in relation to certification for meetings held outside the UK.

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the Prescription Medicines Code of Practice Authority stated that anonymous complaints would be accepted but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties.

It was an established principle under the Code that the UK company was responsible for acts and omissions of its overseas affiliates that came within the scope of the Code. If it were otherwise UK companies would be able to rely on such acts and omissions as a means of circumventing the Code.

Possible reasons for choosing Berlin as a suitable venue given in an internal memo were that Skilarence was approved in Germany and thus it would be compliant to hold a psoriasis related Almirall event there and that Berlin was a well-connected city at a European level. The Panel noted that the largest group of delegates was from Germany.

The Panel noted that there was no evidence that the UK invitees were chosen on the basis of their prescribing of Almirall products. The briefing to the representatives set out the criteria and the nominations were reviewed by the marketing manager and the senior medical advisor. The Panel did not consider that the complainant had provided evidence to demonstrate on the balance of probabilities that the prescribing of Almirall products was the reason for inviting the health professionals. Thus, no breach of the Code was ruled.

The Panel noted that Clause 22.1 stated that hospitality must be strictly limited to the main purpose of the event and must be secondary to the purpose of the meeting ie subsistence only. The level of subsistence offered must be appropriate and not out of proportion to the occasion. Clause 22.1 applied to scientific meetings, promotional meetings, scientific congresses and other such meetings and training. The supplementary information to Clause 22.1 also stated that a useful criterion in determining whether the arrangements for any meeting were acceptable was to apply the question 'Would you and your company be willing to have these arrangements generally known?'. The

impression that was created by the arrangements for any meeting must always be kept in mind. The supplementary information to Clause 22.2 stated that the maximum of £75 plus VAT and gratuities (or local equivalent) did not apply when a meeting was held outside the UK in a European country where the national association is a member of EFPIA and thus covered by EFPIA Codes. In such circumstances, the limits in the host country code would apply. The limit in the German Code was €60 per meal including VAT.

According to the agenda for the meeting as provided by Almirall, it started at 08.15 on Saturday, 27 October and finished at 16.30 with 30 minutes for a morning coffee break and 90 minutes for lunch. The agenda for Sunday, 28 October started at 09.00 where delegates could choose to attend two sessions of parallel workshops followed by 30 minutes conclusion and wrap up finishing the meeting at 11.30. There was no mention on the agenda of the dinners on the Friday and Saturday evenings, nor of the lunch on the Sunday. The meeting schedule provided by the complainant had more detail about the arrangements including those for the dinners on Friday and Saturday and the lunch on Sunday. There was an inconsistency in that the complainant's document stated that the meeting started at 08.30 whereas the company version stated the meeting started at 08.15.

The various groups had dinner by country at different restaurants on the Friday evening and all the delegates had dinner together on the Saturday evening, siting in country groups.

The Panel noted that the cost of the meal on the Friday evening for UK delegates including drinks and taxes was €60 per head as was cost of the dinner on the Saturday evening.

There was no agenda, presentations nor educational content provided on the Friday as alleged. The Panel considered that it was not necessarily unacceptable to offer subsistence to delegates who had arrived the day prior to the meeting. The Panel noted that a buffet lunch was offered on the Sunday. The Panel queried whether the arrangements for the lunch on the Sunday were appropriate noting that it was served 30 minutes after the end of the meeting and cost €42.35 per person including alcohol. In the Panel's view, this was on the limits of acceptability.

The Panel noted Almirall's submission for the arrangements for the dinner on the Saturday evening. It was held in the venue mentioned by the complainant, however, Almirall submitted that the room had been laid out very differently and there was no music or cabaret dancers contrary to the photographs provided by the complainant. The company submitted that no entertainment was provided and that the photographs provided by the complainant were taken at another event at the venue on a different date. The Panel did not consider that the complainant had provided evidence to demonstrate on the balance of probabilities that entertainment other than food and drink was provided.

The Panel considered that it was important for a company to be mindful of the impression created by its activities. Taking all the circumstances into account the Panel did not consider that the hospitality on the Friday, Saturday or Sunday was, on balance, unreasonable. The Panel ruled no breach of Clause 22.1.

The Panel noted its rulings and the lack of evidence. The complainant had not shown that high standards had not been maintained. The Panel ruled no breach of Clauses 9.1 and 2.

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| **Complaint received** | **1 May 2019** |
| **Case completed** | **20 August 2019** |

# ANONYMOUS, NON-CONTACTABLE REPRESENTATIVE v CIPLA

## Conduct of a senior manager

**An anonymous non-contactable individual who described him/herself as being employed by a third party sales organisation which had a contract with Cipla, complained about the conduct of a named senior manager at Cipla who had been in post for some time but had little or no knowledge of the Code and little regard for it. Despite this, he/she controlled the day-to-day workings of representatives.**

**The complainant stated that representatives were asked to put pressure on surgeries to switch patients to Cipla products. The senior manager went to visit customers with representatives and put direct pressure on customers to switch patients. The complainant alleged that at a recent meeting with a named asthma nurse specialist the senior manager was asked if Cipla would sponsor some educational meetings; he/she replied that Cipla would, once it saw an increase in sales in the local area.**

**The complainant alleged that one of his/her colleagues was asked to drive a long distance to see a practice nurse who had a question about the use of an inhaler with a spacer device. The medicine, however, was not licensed for this.**

**The complainant stated that the senior manager regularly played a part at stands in exhibitions, yet had no ABPI qualification.**

**The complainant submitted that the senior manager regularly emailed customers following up on queries that should go to medical information.**

**The detailed response from Cipla is given below.**

**The Panel noted the company's submission that the senior manager was not a representative and there was no need for him/her to take and pass the representative's examination. Cipla decided that the individual would take the examination. On the information provided it appeared that if the senior manager was working as a representative, he/she appeared to be within the timeframe for taking and passing the examination. The Panel did not consider that the complainant had provided evidence to demonstrate on the balance of probabilities that the senior manager was working as a representative and if so that he/she had not met the requirements in the Code for taking and passing the representatives' examination. Thus the Panel ruled no breach of the Code.**

**The Panel noted that there were differences between the complainant's view of the senior manager's activities and Cipla's. The sales strategy to promote cost savings by switching to Cipla's product meant that encouraging switches for existing patients would be part of the representatives' discussions with those upon whom they called. This was not necessarily unacceptable. No evidence had been provided regarding the alleged pressure on representatives to arrange for surgeries to switch nor about the senior manager putting pressure on surgeries to switch. No information was provided about Cipla's involvement in any switch. In relation to the meeting with the asthma nurse specialist, Cipla submitted that the representative had not attended and the senior manager had discussed the company and continuity of supply. There was no mention of a discussion about educational support being linked to increased sales and the complainant had provided no evidence in this regard. The Panel did not consider that the complainant had provided evidence to show that there was a breach of the Code in relation to this aspect of the complaint. No breaches of the Code were ruled.**

**The company submitted that a representative had telephoned the practice nurse who had a question about the use of a spacer device. The complainant had not identified the relevant medicine. Cipla had not provided evidence to show how the representatives were trained on the products. It appeared that some of Cipla's medicines were indicated for use with a spacer and according to Cipla its representatives were fully trained and aware of the licensed indications of its products. The Panel noted that the complainant had provided no evidence that medicines had been promoted in a manner inconsistent with their summaries of product characteristics at the meeting in question and thus ruled no breach of the Code in this regard.**

**The Panel noted that again no evidence had been provided regarding the allegation that the senior manager followed up queries that should be answered by medical information. Cipla had not provided any information about the current arrangement submitting that it was in the process of reviewing and strengthening its process in this regard. The Panel was concerned about the response in relation to this allegation. The company should have a robust process for medical information. However the complainant had not provided any evidence and thus not shown on the balance of probabilities that a breach had occurred. The Panel therefore ruled no breach of the Code in this regard.**

**The Panel did not consider that the complainant had provided evidence to show that the senior manager had promoted medicines at a stand meeting or that any such activity was in breach of the Code. The Panel therefore ruled no breach of the Code.**
**In considering the matters overall, the Panel did not consider that the complainant had shown on the**

**balance of probabilities that there was a breach of Clause 2 of the Code. This clause was used as a sign of particular censure and reserved for such use.**

An anonymous non-contactable individual who described him/herself as being employed by a third party sales organisation which had a contract with Cipla, complained about the conduct of a named senior named manager at Cipla.

**COMPLAINT**

The complainant explained that Cipla employed two sales teams through two named contract sales organisations and that colleagues from both organisations shared his/her concerns. The complainant alleged that the named senior manager at Cipla had little or no knowledge of the Code and little regard for it. Despite this, he/she continued to control the day-to-day workings of representatives.

The complainant stated that representatives were continually being asked to put pressure on surgeries to switch patients to Cipla products. The senior manager went to visit customers with representatives and put direct pressure on customers to switch patients. The complainant alleged that at a recent meeting with an asthma nurse specialist (named) the senior manager was asked if Cipla would sponsor some educational meetings; he/she replied that Cipla would, once it saw an increase in sales in the local area.

The complainant alleged that one of his/her colleagues was asked to drive a long distance to see a practice nurse who had a question about the use of an inhaler with a spacer device. The medicine, however, was not licensed for this and so the representative should not have been asked to do that.

The complainant stated that the senior manager regularly played a part at stands in exhibitions, yet had no ABPI qualification. Once introduced to customers he/she would often then take on a relationship with that customer and cut the representative out.

The complainant submitted that the senior manager regularly emailed customers following up on queries that should go to medical information. The complainant stated that he/she and his/her colleagues had complained to management at the third-party contract sales organisations but they did not do anything because they might lose the business.

When writing to Cipla, the Authority asked it to consider the requirements of Clauses 2, 3.2, 9.1, 16.3 and 19.2 of the 2016 Code.

**RESPONSE**

Cipla submitted that the named senior manager had been employed by Cipla for over five years in various roles. Details were provided.

Cipla submitted that the manager was not a representative as defined in Clause 16, however the expectation was that he/she would pass the ABPI examination within two years. He/she planned to take the examination shortly (details provided).

Cipla stated that neither third party had received any formal internal complaints about the manager. However, as a precaution the manager had been asked to step back from initiating any direct contact with the contract sales force until he/she had sat the ABPI examination. Details of his/her relationship with the third party organisation were provided.

With regard to the senior manager's knowledge of the Code, Cipla stated that when he/she started work with the company it conducted an 'Overview of the Code' training session led by the medical signatory. Cipla submitted that the manager was not a representative as defined in Clause 16.3 and so he/she knew that he/she should not conduct customer facing activities. Given his/her role he/she took an interest in the sales teams and would accompany sales calls and interact with the representatives from both outsource companies.

With regard to the alleged pressure on representatives to get surgeries to switch to Cipla medicines, Cipla explained that the contract sales organisations promoted Sereflo (salmeterol/fluticasone propionate) and Kelhale (beclomethasone dipropionate). Both had a value-based message and details of the strategy was provided. Training materials, promotional materials and briefing documents were all certified and in place.

Cipla submitted that the senior manager had accompanied calls, as an observer, to understand how the sales strategy was received. He/she did not have the relevant training to be a sales representative for Cipla.

The meeting with the asthma nurse specialist was set up by a representative and the senior manager was due to accompany this call to ensure that Cipla as a company was introduced. The representative could not attend and the manager ended up in the meeting alone, which could have been avoided. The conversation, however focused on the company and its capability for continuity of supply.

Cipla acknowledged that the manager had contacted a representative in one area about an issue in another, and the representative agreed to call the practice to resolve the issue, rather than drive. The sales team was fully trained and knew the licensed indications for Cipla brands and which could be used with spacers and which could not. Cipla submitted that this was covered in their training and summary of products characteristics (SPC) validations and that the contract sales organisation's inputs corroborated this.

With regard to exhibition stands, Cipla submitted that since November 2018, a formal process had been in place for stand meetings to be approved centrally, so it had visibility on all of those activities. Cipla ensured that it always had ABPI qualified representatives to man the stand. The manager could attend relevant meetings, but not as a representative of the company as detailed above.

The manager was aware that he/she could not act as a representative of Cipla as defined by Clause 16. He/she did accompany calls and took an active interest in the sales strategy.

With regard to the allegation that the manger followed up queries, Cipla stated that the medical information process would be reviewed including the execution done to date. Irrespective of the review outcome, the company would work to strengthen the implementation of the process for all employees in the course of the next four months.

Cipla submitted that the contract sales organisations had confirmed that no employee had raised any of the comments made by the complainant.

Cipla denied that it had breached Clause 2 as the intention of its senior management team was to abide by the Code in all interactions with health professionals.

Cipla noted that Clause 3.2 required that the promotion of a medicine must be in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its SPC. Cipla submitted that the contract sales team had been appropriately trained and validated on the SPCs for the products promoted.

With regard to the maintenance of high standards, Cipla submitted that it had a strong internal code of conduct, similar to the principles in the Code.

Cipla reiterated that the senior manager was not employed as a representative; he/she was a senior manager in the UK business, and so Clause 16.3 did not apply to him/her.

With regard to the conversation with the asthma nurse specialist and the alleged conditional offer to sponsor educational meetings, Cipla refuted that any conversations about medical and educational goods and services (MEGS) took place; Cipla did not have any MEGS activities in place.

**PANEL RULING**

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the PMCPA stated that anonymous complaints would be accepted but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant had provided no evidence to support his/her allegations and could not be contacted for more information.

The Panel noted Cipla's submission that the senior manager was not a representative. The definition of a representative was given in Clause 1.7 of the Code as a representative calling upon members of the health professions and other relevant decision makers in relation to the promotion of medicines. Given the company's submission about the senior manager's role, it was difficult to see why the senior manager needed to accompany representatives on calls. The company submitted that this was to observe the representative whereas the complainant took a different view. The senior manager had conducted a meeting with a health professional which was said to focus on discussions about the company and the continuity of supply. The Panel considered that this was likely to be a discussion within the definition of promotion given in Clause 1.2 of the Code as any activity which promotes the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines.

The Panel noted the company's submission that the senior manager was not a representative and there was no need for him/her to take and pass the representative's examination. Cipla decided that the individual would take the examination and in the interim would not have direct contact with the sales force until he/she had taken the examination. The Panel noted the company's submission about when the senior manager's role commenced and when he/she was planning to take the examination. The Panel had no information before it as to the senior manager's activities in his/her previous role at Cipla UK. On the information provided it appeared that if the senior manager was working as a representative, he/she appeared to be within the timeframe for taking and passing the examination. The Panel did not consider that the complainant had provided evidence to demonstrate on the balance of probabilities that the senior manager was working as a representative and if so that he/she had not met the requirements in the Code for taking and passing the representatives' examination. Thus the Panel ruled no breach of Clause 16.3.

The Panel noted that there were differences between the complainant's view of the senior manager's activities and Cipla's. The sales strategy to promote cost savings by switching to Cipla's product meant that encouraging switches for existing patients would be part of the representatives' discussions with those upon whom they called. This was not necessarily unacceptable. No evidence had been provided regarding the alleged pressure on representatives to arrange for surgeries to switch nor about the senior manager putting pressure on surgeries to switch. No information was provided about Cipla's involvement in any switch. In relation to the meeting with the asthma nurse specialist, Cipla submitted that the representative had not attended. The senior manager had according to Cipla discussed the company and continuity of supply. There was no mention of a discussion about educational support being linked to increased sales and the complainant had provided no evidence in this regard. The Panel did not consider that the complainant had provided evidence to show that there was a breach of the Code in relation to this aspect of the complaint. No breach of Clauses 9.1 and 19.2 of the Code was ruled.

The company submitted that a representative had telephoned the practice nurse who had a question about the use of a spacer device and not driven as alleged. The complainant had not identified the

relevant medicine. Cipla had not provided evidence to show how the representatives were trained on the products. It appeared that some of Cipla's medicines were indicated for use with a spacer and according to Cipla its representatives were fully trained and aware of the licensed indications of its products. The Panel noted that the complainant had provided no evidence that medicines had been promoted in a manner inconsistent with their SPCs at the meeting in question and thus ruled no breach of Clause 3.2 of the Code in this regard.

The Panel noted that again no evidence had been provided regarding the allegation that the senior manager followed up queries that should be answered by medical information. Cipla had not provided any information about the current arrangement submitting that it was in the process of reviewing and strengthening its process in this regard. The Panel was concerned about the response in relation to this allegation. The company should have a robust process for medical information. However the complainant had not provided any evidence and thus not shown on the balance of probabilities that a breach had occurred. The Panel therefore ruled no breach of Clause 9.1 of the Code in this regard.

The Panel noted that the senior manager attended meetings where exhibition stands were used and Cipla's submission that the senior manager was not attending as a representative. It was not clear exactly what role the senior manager would have at such meetings. The Panel did not consider that the complainant had provided evidence to show that the senior manager had promoted medicines at a stand meeting or that any such activity was in breach of the Code. The Panel therefore ruled no breach of Clause 9.1 of the Code.

In considering the matters overall, the Panel did not consider that the complainant had shown on the balance of probabilities that there was a breach of Clause 2 of the Code. This clause was used as a sign of particular censure and reserved for such use.

**Complaint received** **9 May 2019**

**Case completed** **20 August 2019**

**CASE AUTH/3205/6/19**

# VOLUNTARY ADMISSION BY BOEHRINGER INGELHEIM

## Lack of certification and obligatory information

**Boehringer Ingelheim admitted breaches of the Code in that e-learning material for the Respimat device, was made live on a third party agency's website before it had been certified. In addition, the agency involved which was contracted by Boehringer Ingelheim emailed health professionals on its database alerting them to the material. Boehringer Ingelheim had no prior knowledge of, nor had it approved/certified, the promotional email. The email sent by the agency did not contain prescribing information or other obligatory information for promotional materials. The Respimat device was a type of inhaler used for several Boehringer Ingelheim respiratory medicines.**

**As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Boehringer Ingelheim.**

**The detailed response from Boehringer Ingelheim is given below.**

**The Panel noted that instead of one piece of material ('How to use' downloadable pdf), the agency uploaded the whole e-learning course to its live website. The emails between the agency and Boehringer Ingelheim were confusing and not particularly clear in relation to what had and what had not been approved. The emails showed that Boehringer Ingelheim was asked to check the website and confirm that it was ready to make the course live in a particular area for a three-month trial. In the Panel's view, given the content of the correspondence from Boehringer Ingelheim, it was not unreasonable for the agency to assume that it could make the whole e-learning course live.**

**The Panel noted that Boehringer Ingelheim described the material for the website as educational and non-promotional in nature to assist pharmacists with supporting patients who might be on a product using a Respimat device. Three Boehringer Ingelheim products were available in this device, Spiolto (tiotropium and olodaterol), Spiriva (tiotropium) and Striverdi (olodaterol).**

**The Panel noted that although some of the materials for the e-learning had been approved individually for different uses, such as in sales aids, the material made available on the website had been published prior to certification for such use by Boehringer Ingelheim. The Panel therefore ruled a breach of the Code as acknowledged by the company.**

**The Panel noted that the agency had also emailed those registered on its database. The email referred to the training course 'How to support patients with a Spiriva Respimat Device'. The Panel noted that the agency did not appear to have contacted Boehringer Ingelheim about the email; the agency had let down Boehringer Ingelheim in that regard. The email had not been certified and did not meet the requirements for the provision of prescribing information. In addition, the email did not include the required statement regarding the reporting of adverse events and the non-proprietary name was not adjacent to the first appearance of the brand name. Although the date of sending the email was included on the email it was not clear whether this was the date that the content was drawn up. The Panel therefore ruled breaches of the Code as acknowledged by the company.**

Boehringer Ingelheim Limited admitted breaches of the Code in that e-learning material for the Respimat device was released for use before it had been certified, and an email alerting health professionals to the material did not contain prescribing or other obligatory information.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Boehringer Ingelheim.

**VOLUNTARY ADMISSION**

Boehringer Ingelheim submitted that in April 2019, its ethics & compliance team was alerted to a potential non-compliance with the Code and so it started its investigatory procedure. Immediate corrective actions to rectify the situation were taken as detailed below.

Boehringer Ingelheim stated that its investigation established that:

- A third party agency was contracted by Boehringer Ingelheim to develop an e-learning course for local pharmacists related to education materials on the Respimat device, an inhaler type used for several Boehringer Ingelheim respiratory medicines. Before any activity, Boehringer Ingelheim required the agency to undertake Code training, which had happened.

- The e-learning materials proposed to be added to the third party agency website were in the development/certification process by Boehringer Ingelheim following its documented procedures.

- Unfortunately, the agency made the e-learning course live on its website before it had all been certified. Before the agency did that, it emailed Boehringer Ingelheim to ask if the e-learning training could go live, and a member of staff emailed back to confirm that it could. However, there was a misunderstanding as to what was being made live – the member of staff

thought that the agency had only referred to a downloadable pdf (the only part of the e-learning course which had been certified for that purpose), which was in fact the subject heading of the email chain.

- Unfortunately, the agency interpreted the email as confirmation of being able to go live with the entire e-learning course. When it went live on the agency website, not all of the e-learning material had been certified with this intent (in breach of Clause 14.1).

- The agency emailed health professionals on its database to invite them to take the Respimat e-learning course. Boehringer Ingelheim had no prior knowledge of nor had it approved/certified the promotional email. The email sent by the agency did not contain prescribing information or other obligatory information for promotional materials (in breach of Clauses 14.1, 4.1, 4.3, 4.8 and 4.9).

Boehringer Ingelheim stated that the agency was immediately instructed to remove the whole website from live status so that it was no longer visible. This was confirmed as completed on the same day that the non-compliance was identified by Boehringer Ingelheim.

The final investigation report, following a comprehensive process where all relevant parties were interviewed, was presented to the Compliance Investigation Review Committee in May. The Committee would decide on any formal action. The report would be sent to the country managing director, the medical director and the head of ethics & compliance.

Boehringer Ingelheim submitted that whilst it wished to complete its investigation swiftly, as it needed to investigate the processes undertaken by both the company and the agency and undertake extensive interviews, it had taken some time to complete the process. Additionally, it had also reviewed similar programmes supported by Boehringer Ingelheim to be assured of compliance with the Code; the non-compliance reported here appeared to be an isolated incident.

The root cause of this non-compliance could be summarised as a misunderstanding involving the agency and a member of staff as to what had been certified and secondly the agency inappropriately emailing pharmacists without either permission or knowledge of Boehringer Ingelheim.

In addition to the immediate corrective actions which ensured compliance and no further activity on this project, other preventative actions included specific re-training for relevant staff and details were provided.

Boehringer Ingelheim stated that it took compliance with the Code very seriously. It was committed to enhancing the quality and compliance of its interactions with third parties and with health professionals and considered that robust certification underpinned effective self-regulation.

Boehringer Ingelheim noted that despite insisting on Code training in advance of starting work, it felt let down by the agency particularly with respect to the second root cause as listed above. As soon as the company knew about the situation it put in place the corrective and preventative actions (CAPA) as summarised above.

Boehringer Ingelheim was asked to provide the Authority with any further comments in relation to the requirements of Clauses 4.1, 4.3, 4.8, 4.9 and 14.1 of the Code.

**RESPONSE**

Boehringer Ingelheim explained that in early 2018, the respiratory team discussed a project with a third party agency to help deliver educational training on the Respimat inhaler device to pharmacists in a named area. A brief was provided to Boehringer Ingelheim by the agency.

As Boehringer Ingelheim had not worked with the third party agency before, it mandated that the agency demonstrate Code knowledge before any activity started. Details were provided. The contract with the agency included the requirements for compliance with the ABPI Code and mandatory Boehringer Ingelheim Code.

An extension of the contract was required as there had been significant change in the Boehringer Ingelheim respiratory marketing team. The project was therefore put on hold, although a 'How to use' downloadable pdf was asked to be put through the approvals process.

In February 2019, a Boehringer Ingelheim member of staff emailed the agency to let it know that a 'How to use' downloadable pdf had now been certified specifically for the website. This was the only component of the project that this member of staff had been asked to assist with. Over the course of the next few days, the email chain continued. The subject title of the email chain throughout was 'Downloadable HowTo Use Page – Approved for use'. It was unfortunately this e-mail chain misunderstanding that led the agency to consider that the whole website could go live, whereas the Boehringer Ingelheim member of staff only meant to confirm that this specific element was approved. It should also be noted that the member of staff's involvement was limited to facilitating the certification of the downloadable pdf, to which he/she thought the email conversation still related.

The live status of the website only became clear to Boehringer Ingelheim on 2 April 2019, when a manager was tasked with resuming the project. In talking to the agency, he/she was shocked to hear that the e-learning course had been live since 1 March 2019, by which time several pharmacists had already accessed it. The manager alerted another manager, who convened an urgent meeting to understand the situation, called the agency to request the website be immediately removed from public view and alerted the ethics & compliance department.

Boehringer Ingelheim summarised the content of the e-learning course which it submitted was intended to be educational and non-promotional and assist pharmacists in supporting patients who might be using the Respimat device, a soft mist type of inhaler.

Despite the content of the e-learning being educational and never intended to go live before certification, in the spirit of self-regulation Boehringer Ingelheim accepted that the website became accessible before certification and so for the short duration it was live, was in breach of Clause 14.1 of the Code.

After Boehringer Ingelheim found out about the website going live on 2 April 2019, it became apparent that the agency had proactively and without Boehringer Ingelheim's knowledge or permission alerted its database of registered pharmacists to courses on its website. This included Boehringer Ingelheim's Respimat device training. The mailing was sent on 7 March 2019.

Boehringer Ingelheim provided metrics from the agency in relation to the numbers sent the email, opened it, looked at the course and completed it.

As noted above, Boehringer Ingelheim stated that it was let down on this specific element that despite insisting on Code training in advance of starting any work, the agency failed to get the company's permission or even inform it of its plans to send a mailing to its registered pharmacist database.

Boehringer Ingelheim nonetheless accepted that it had to take responsibility for the actions of any third parties acting on its behalf and therefore in the spirit of self-regulation it accepted that the mailing was not certified, in breach of Clause 14.1. Furthermore, as the Respimat course referred to Spiriva (tiotropium) Respimat and as the mailing was sent without reference to prescribing information and other required information, the mailing was also in breach of Clauses 4.1, 4.3, 4.8 and 4.9 of the Code.

Boehringer Ingelheim stated that it strove at all times to comply with the spirit and letter of the Code. The company had ensured the contract with the agency could not proceed until the agency had demonstrated recent training in the Code, which it had undertaken.

Furthermore, Boehringer Ingelheim noted that it had taken immediate (same day) corrective actions to re-establish compliance and had further preventative actions to minimise the risks of this occurring again, as outlined above.

Boehringer Ingelheim acknowledged that it was of paramount importance to maintain high standards at all times and it sincerely apologised for the unfortunate situation which arose from two root causes for which it put in place a robust CAPA.

**PANEL RULING**

The Panel noted that instead of one piece of material ('How to use' downloadable pdf), the third party agency uploaded the whole e-learning course to its live website. The emails between the agency and a Boehringer Ingelheim member of staff were confusing and not particularly clear in relation to what had and what had not been approved. The emails showed that Boehringer Ingelheim was asked to check the website and confirm that it was ready to make the course live across pharmacies in a particular area for a three-month trial. In the Panel's view, given the content of the correspondence from Boehringer Ingelheim, it was not unreasonable for the agency to assume that it could make the whole e-learning course live.

The Panel noted that there was some confusion as to whether the materials for the e-learning were promotional or not.

The Panel noted that Boehringer Ingelheim described the material for the website as educational and non-promotional in nature to assist the pharmacists with supporting patients who might be on a product using a Respimat device. Three Boehringer Ingelheim products were available in this device, Spiolto (tiotropium and olodaterol), Spiriva and Striverdi (olodaterol).

Boehringer Ingelheim submitted that some of the individual items were non promotional; it accepted that the failure to certify the e-learning was a breach of Clause 14.1 of the Code. This clause referred to the need to certify promotional material. According to the response from Boehringer Ingelheim the landing page for the e-learning stated 'How to support patients with a Spiriva Respimat Device' followed by 'Do you know how to load, prime and use the Spiriva Respimat device and can you help your patients?' and 'Do you know why particle size and velocity is important in an inhaler?' Some of the material referred only to the Respimat device, in that regard the Panel noted the supplementary information to Clause 4.1 Advertisements for Devices referred to advertisements relating to the merits of a device used for administering medicines, such as an inhaler, which was supplied containing a variety of medicines, the prescribing information for one only need be given if the advertisement made no reference to any particular medicine. The Panel noted that it appeared from the correspondence that the company expected prescribing information to be used on the website.

The Panel noted that although some of the materials for the e-learning had been approved individually for different uses, such as in sales aids, the material made available on the website had been published prior to certification for such use by Boehringer Ingelheim. The Panel therefore ruled a breach of Clause 14.1 of the Code as acknowledged by the company.

The Panel noted that the agency had also sent an email to people registered on its database. The email referred to the training course 'How to support patients with a Spiriva Respimat Device'.

The Panel noted that the agency did not appear to have contacted Boehringer Ingelheim with regard to the email and considered that Boehringer Ingelheim

had been let down by its agency in that regard. The email had not been certified and did not meet the requirements for the provision of prescribing information. In addition, the email did not include the required statement regarding the reporting of adverse events and the non-proprietary name was not adjacent to the first appearance of the brand name. Although the date of sending the email was included on the email it was not clear whether this was the date that the content was drawn up. The Panel therefore ruled a breach of Clauses 14.1, 4.1, 4.3, 4.8 and 4.9 as acknowledged by the company.

| | |
|---|---|
| **Complaint received** | **11 June 2019** |
| **Case completed** | **10 September 2019** |

**CASE AUTH/3208/6/19**

# MEMBER OF THE PUBLIC v MERZ

## Alleged promotion on Instagram

**A complaint was received from a contactable member of the public who indicated that he/she worked for a body contouring company. The complainant alleged that a named representative from Merz Pharma UK had used an Instagram account to promote Bocouture (botulinum toxin type A). Bocouture was indicated for the temporary improvement in the appearance of certain upper facial lines.**

**The complainant provided copies of images downloaded from an Instagram account in which a representative from Merz had created his/her own account under the company's name and had actively promoted Bocouture on the account. Bocouture was a prescription-only medicine.**

**The detailed response from Merz is given below.**

**The Panel noted that the Instagram account was set up by a Merz representative for business purposes. This appeared to be contrary to the Merz policy on social media based on the extracts from the company handbook provided by Merz.**

**The Panel queried why another representative was to communicate to the representative in question that the images on the Instagram profile should be removed. It was not known whether this had happened. In any event removal of the images would leave the account still running. It was not clear whether this would be in line with the policy given that using personal social media accounts for business purposes was reported as being contrary to the Merz policy.**

**The Panel was also concerned that checking that the images had been removed was left to a junior person and not a member of staff responsible for representatives. It was only when a manager was made aware some days later that an image of Bocouture could be seen that the matter was escalated. Following this all representatives were asked to confirm by email that they did not hold active business social media accounts containing product details.**

**The Panel considered that although the Instagram post was primarily about medical devices and encouraged viewers to be ready for summer, the pack shot of Bocouture, a prescription only medicine, would be seen as part of that message ie that the products illustrated were available to viewers to be 'summer ready'. In this regard the Panel considered that the Instagram post was an advertisement.**

**The Panel noted that the privacy arrangements for the account in question were not clear. Nor was it clear who followed the account. Merz submitted that the followers were Merz colleagues, healthcare professionals and other relevant decision makers. On the balance of probabilities, the Panel concluded that the Instagram account was not private. Anyone, including members of the public would be able to view it.**

**The Panel considered that including a pack shot of a prescription only medicine on the Instagram account in a positing which advertised other Merz products meant that Bocouture, a prescription only medicine, was being advertised to the public. The Panel therefore ruled a breach of the Code.**

**The representative in question had failed to maintain a high standard of ethical conduct and a further breach was ruled. The Panel noted Merz's submission that it had a policy that employees were not to use personal social media accounts for business purposes but nevertheless considered that the company had failed to maintain a high standard given the initial failure to properly review the material and identify that the product images included a prescription only medicine and the delay between being notified about the Instagram account and the instruction for the profile to be deleted. It was also concerning that juniors were asked to deal with the matter. The Panel therefore ruled a breach as high standards had not been maintained.**

**The Panel did not consider that the complainant had shown on the balance of probabilities that there was a breach of Clause 2 of the Code.**

A complaint was received from a contactable member of the public who indicated that he/she worked for a body contouring company. The complainant alleged that a named representative from Merz Pharma UK Ltd had used an Instagram account to promote Bocouture (botulinum toxin type A). Bocouture was indicated for the temporary improvement in the appearance of certain upper facial lines.

**COMPLAINT**

The complainant provided copies of images downloaded from an Instagram account in which a representative from Merz had created his/her own Instagram account under the company's name and had actively promoted Bocouture on the account. Bocouture was a prescription-only medicine.

When writing to Merz, the Authority asked it to consider the requirements of Clauses 2, 9.1, 15.2 and 26.1 of the Code.

**RESPONSE**

Merz referred to the complainant as an ex-employee. The company explained that at a Merz educational meeting on 13 June, a manager was

told by a colleague (another representative) that the representative named by the complainant had set up a Merz profile on Instagram and had imported images of the dermal fillers Belotero and Radiesse, both of which were medical devices. It was discussed that some customers preferred to use the direct messaging function of Instagram as an effective way to communicate meeting arrangements and other business logistics vs email or conventional texting, and this was why the representative in question set up the account.

The manager was also made aware that a director and another manager had advised the representative that under no circumstances were Merz employees to use personal social media accounts for business purposes and that they should refer to the Policy on Social Media as outlined in the company handbook.

The manager was assured that his/her colleague would tell the representative immediately that the images on the Instagram profile should be removed. The manager's motive was based on the fact that he/she clearly understood that any images of product sourced direct by any staff member that had not been through the formal approval process should not be used in social media (or any form of communication).

The next morning, whilst on annual leave, the manager asked a junior person to review the representative's Instagram profile and confirm that all images of product had been removed. As the images seen on the grid view were only recognised as Belotero and Radiesse so not prescription-only medicines, the action was not deemed urgent and, due to resourcing pressures and workload, other work was prioritised. A meeting between the manager and junior person was scheduled for Wednesday, 19 June when it was agreed that the matter would be discussed further.

Merz stated that during the two weeks spanning the period in question, the marketing team responsible for the injectables portfolio (Belotero, Radiesse and Bocouture) executed a number of events which relied heavily on the manager and junior person and the vacancies in the team, intensified pressure during this period. Due to these distractions the representative's Instagram account was not checked and the image in question remained undetected.

At the meeting on 19 June the manager was told that the images had not been removed and that if the images on the grid view were enlarged, a pack shot of Bocouture could be seen. This information was immediately escalated to another manager in order to instruct the representative to immediately delete his/her profile. This was actioned that afternoon and no further viewing of the profile was possible. The manager received written confirmation of the deletion of the account from the representative that evening.

In parallel with this activity, the complainant contacted the PMCPA on 18 June and Merz received the complaint on 20 June. The sales managers were immediately contacted by medical affairs who requested that, as a matter of urgency, all representatives confirmed by email that they did not hold active business social media accounts containing product details. Sales managers were also briefed to remind their teams to contact themselves, medical affairs or refer to the company handbook for details of the Merz Social Media Policy if they had any immediate questions. In addition, a full audit of all Merz staff for any social media accounts was undertaken; no accounts identified contained product promotion of a prescription only medicine.

Merz submitted that the Instagram profile in question was initially examined on the 'tile view' where it was noted that a series of pack shots of products as part of a collection of photographs had been uploaded. There were four photographs on the page including images of Merz colleagues and pack shots of Radiesse and Belotero. One of the tiles showed seven packs – six of these were Belotero and one was Bocouture. The images uploaded were not from the Merz bank of certified and approved pack shots and company policy was very clear that all product-related communications, including any images, must be certified and approved through the Merz approval system, regardless of whether they were prescription only medicines or medical devices. Merz noted that there were only four images on the account (normally nine could be seen) which illustrated the relative newness of it. It was active for just six days.

Merz stated that the representative had looked at similar accounts held by employees of two other manufacturers in aesthetic medicine and sought to recreate their page layout and look. The representative had then searched Instagram for 'Belotero' and copied some of the photographs found under the hashtag #beloterofiller. This was not an official or approved Merz hashtag and the photograph chosen was from a German healthcare professional. The representative's focus was on the dermal filler Belotero and the caption below (not shown in full in the complaint letter) made this clear:

> 'Summer is on the way! Are you Ready…
>
> Patients today don't want a filler that "owns" them; they want a filler that naturally integrates into their tissue, so that they can retain their identity and express their emotions with confidence.
>
> Thanks to the Belotero portfolio of fillers, it's possible to tailor a personal treatment protocol for every patient, so that they can feel empowered, own their age and own their beauty.'

This was approved copy that the representative had lifted from the Merz Belotero website. Belotero was a medical device and so promotion of it fell outside the Code.

Merz noted that in the tile view (four images on a mobile device screen) the Bocouture pack (around half the size of the other packs) was less obvious and set against a dark background. In addition, the image resolution made the brand name difficult

to read and so those viewing the page who were not health professionals would not easily see the Bocouture brand name. If this image alone was selected (and viewed in full screen mode) the Bocouture pack was only 6mm x 8mm (on a standard smart phone screen). Further, given that the accompanying text exclusively referred to a dermal filler the complainant's allegation that the representative had actively promoted Bocouture was misleading.

Merz noted its company culture regarding the intrinsic regard for the Code across the entire business and the training processes rigorously implemented and adhered to throughout the organisation as outlined below.

The Merz Company Handbook, which was trained out to all employees when they started employment with Merz, clearly outlined the company policy on the use of social media. On the business use of social media the guidance was as follows:

> 'If your duties require you to speak on behalf of the organisation, this does not automatically give you the authority to do so in a social media environment. Discussion of the company or any information relating to the Company in a social media environment is not permitted unless specifically authorised by your line manager or a member of the Management team' … 'You should not presume that content generated will remain private' … 'You should contact your colleagues and/or relevant experts if you plan to generate content within social media relating to the company to ensure content is accurate and not infringing any third party rights.'

Merz medical affairs regularly presented updates on the Code to the sales teams at regional and team meetings. All permanent members of the promotional team had to undertake the ABPI examination and were regularly coached in the field by the Merz training manager and sales managers.

Merz had taken this opportunity to review its current processes and to clarify policy where it considered that it might be required. Additionally, an email was sent to UK employees about the use of social media and this topic would be discussed with employees again at the upcoming sales meeting in July.

**Clause 26.1 (advertising to the public)**

Merz considered two perspectives; intent and definition/interpretation.

Merz submitted that:

1 Intent – based on a meeting with the representative and the wording on the Instagram page (that pre-dated the complaint) it was clear that the Instagram account was intended to serve as a communication portal with Merz colleagues, other relevant decision makers and healthcare professionals only and to highlight only the dermal filler Belotero. The 57 followers of the representative's account were audited and they exclusively comprised the above categories; there were no members of the public. Accordingly, there was no opportunity for the post to be seen by the public.

2 Definition/interpretation (of advertising) – the Code defined 'promotion' but not (explicitly) 'advertising'. Clauses 5 and 6 detail the requirements for advertisements and these, importantly, furnish the viewer with enough information to make an informed decision to administer, consume, prescribe, purchase, recommend, sell, supply or use a medicine. Merz submitted that for an image to act as an advertisement there must be the context for a viewer to become influenced to act. The presence of a pack image only with a brand name that, even in expanded view, had letter heights smaller than 2mm, suggested that the ability of the viewer to discern what was shown as a prescription only medicine was negligible (unless they were a health professional with prior contextual knowledge).

In view of the above, Merz submitted that the inclusion of the small pack image of Bocouture without any other information and accompanying text that referred exclusively to a dermal filler to a group of individuals who were exclusively industry members, health professionals or other relevant decision makers supported that the Instagram posting could not constitute advertising to the public and therefore Clause 26.1 had not been breached.

**Clause 15.2 (high standard of ethical conduct for representatives)**

Recognising the relatively narrow definition of Clause 15.2 (which related to ethical standards) Merz noted the representative's behaviour and subsequent co-operation with the internal investigation, and the culture of the organisation which was driven and reinforced with a high degree of regularity from both a corporate and local leadership perspective. One of the company values was to 'Deliver trusted results'. Merz noted that part of the supporting sub-text stated:

> 'Quality, ethics and excellence are at the heart of what we do, patients really matter and we will always be honest.'

At a local level the managing director for Merz UK personally took all new employees through an induction process that included the company's values and also reinforced the mantra which stated that Merz would never compromise patient safety or mislead health professionals. This was widely understood by all staff and empowered them to act when they considered that these standards were not being upheld.

Since Clause 15.2 was specific to 'ethical' conduct, Merz did not consider that the representative's actions were unethical. As the representative acted in a way that he/she thought was morally right and made an honest mistake in including a photograph of a medicine it was difficult to see these actions

as immoral. The representative was sincerely apologetic and his/her remorse supported the point that he/she recognised his/her error and that his/her moral compass was genuine and appropriate for the industry.

**Clause 9.1 (high standards)**

Merz noted that since it was set up in 2006, compliance, standards and ethical behaviour were a cornerstone of the way it did business. As the complainant was an ex-employee who would have been privy to all commercial briefings, (and therefore able to cite clear breaches had the culture been such), should support that fact that Merz took compliance seriously. Merz noted that the Instagram account was first established on 13 June, first identified as containing an errant Bocouture carton on 19 June and suspended immediately, that same day, and the matter promptly escalated to the representative's line manager for disciplinary review. All of this happened before the complaint arrived on 20 June. The presence of clear guidance and training on the use and associated risks of social media, the speed of response and empowerment of a junior member of staff to act swiftly to remedy the matter indicated that clear professional standards and effective processes were in place. The fact that a full audit of all Merz staff social media accounts failed to identify further cases confirmed this was an isolated incident. In this regard, Merz submitted that high standards had been maintained.

**Clause 2 (bringing the industry into disrepute)**

Since Clause 2 was a sign of particular censure, reserved for serious, multiple or repeated breaches, Merz submitted that this single alleged promotion on Instagram did not constitute such a breach.

In summary, Merz noted that it had had little interaction with the Panel for many years which reflected its culture and systems. As a small company its resources were limited, however, it prioritised compliance and its culture and intent was genuine. The complaint had served as a useful reminder to the organisation of why compliance was important and it would use it as an internal case study across the business to reinforce ethical and compliant behaviours.

**PANEL RULING**

The Panel noted that Merz referred to the complainant as an ex-employee. The complainant however, described him/herself in such a way that the Panel considered him/her to be a member of the public.

The Panel noted that the Instagram account was set up by a member of the Merz sales team, a representative, for business purposes. This appeared to be contrary to the Merz policy on social media. The Panel was not provided with a copy of a policy but was provided with extracts from the company handbook which Merz submitted clearly outlined the company policy on the use of social media.

The Panel queried why another sales representative was to communicate to the representative in question that the images on the Instagram profile should be removed. It was not known whether this had happened. In any event removal of the images would leave the account still running. It was not clear whether this would be in line with the policy given that using personal social media accounts for business purposes was reported as being contrary to the Merz policy. The company also submitted that the policy stated that the use of social media for discussion of the company or any information relating to the company in a social media environment was not permitted unless specifically authorised by the line manager or member of the management team.

The Panel was also concerned that checking that the images had been removed was left to a junior person and not a member of staff responsible for representatives and that the images were only looked at in the grid view. It was only when a manager was made aware some days later that an image of Bocouture, a prescription only medicine, could be seen that the matter was escalated to the sales manager. Following this all representatives were asked to confirm by email that they did not hold active business social media accounts containing product details. The full audit of Merz staff was reported as confirming that no accounts identified contained promotion of a prescription only medicine. The Panel noted Merz's submission that the account in question was new and active for just six days.

The Panel noted Merz's submission that when four images were viewed on tile view on a mobile phone, the Bocouture pack, which was around half the size of the six other packs shown, was small and the brand name difficult to read. The six other packs were products from the Belotero range. Merz submitted that these were medical devices (fillers) and thus not covered by the Code.

The Panel considered that although the Instagram post was primarily about the medical devices and encouraged viewers to be ready for summer, the pack shot of Bocouture, a prescription only medicine would be seen as part of that message ie that the products illustrated were available to viewers to be 'summer ready'. In this regard the Panel considered that the Instagram post was an advertisement.

The Panel understood that whether the Instagram post was available to the public would depend on the privacy settings of the account. Instagram was said to be a photo/video sharing site. Business profiles were not able to be made private. It appeared that by default, anyone could see a person's profile and posts on a personal account. Personal accounts could be made private so that only followers approved by the account holder could see what that account holder shared. If an account was set to private, only approved followers would see the photos or videos on hashtag or location pages. Only those accepted by the account owner would be able to see the postings. This appeared to the Panel to be different to the arrangements for some other social media platforms.

The complainant stated that he/she came across the Instagram account online. The account details indicated that there were '57 followers 131 following'. The Panel noted that the privacy arrangements for the account in question were not clear. Nor was it clear who followed the account. Merz submitted that the followers were Merz colleagues, healthcare professionals and other relevant decision makers. There was a difference between potential audiences with regard to advertising prescription only medicines and advertising medical devices. It was not clear from either the complainant or Merz whether it was appropriate to advertise a prescription only medicine to all the followers. Although the account was a personal account it was set up for business purposes and was therefore likely to be more useful if it were available to anyone to view. In addition, from the photograph provided by the complainant, which included an option to follow the account, it appeared to the Panel that the complainant was not following the account. The photograph provided by the complainant included the pictures in tile view and it appeared that the complainant would be able to click on each tile to view the enlarged version. The complainant provided a photograph of the enlarged version. On the balance of probabilities, the Panel concluded that the Instagram account was not private. Anyone, including members of the public would be able to view it.

The Panel considered that including a pack shot of a prescription only medicine on the Instagram account in a positing which advertised other Merz products meant that Bocouture, a prescription only medicine, was being advertised to the public. The Panel therefore ruled a breach of Clause 26.1.

The Panel considered that the representative in question had failed to maintain a high standard of ethical conduct and ruled a breach of Clause 15.2. The Panel noted Merz's submission that it had a policy that employees were not to use personal social media accounts for business purposes but nevertheless considered that the company had failed to maintain a high standard given the initial failure to properly review the material and identify that the product images included a prescription only medicine and the delay between being notified about the Instagram account and the instruction for the profile to be deleted. It was also concerning that juniors were asked to deal with the matter and one of them did not appear to have sufficient knowledge to deal with the matter. The Panel therefore ruled a breach of Clause 9.1.

In considering the matters overall, the Panel did not consider that the complainant had shown on the balance of probabilities that there was a breach of Clause 2 of the Code. This clause was used as a sign of particular censure and reserved for such use.

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| **Complaint received** | **19 June 2019** |
| **Case completed** | **12 September 2019** |

**CASE AUTH/3210/6/19**

# PATIENT v GLAXOSMITHKLINE

## Alleged out-of-date patient material

**An anonymous, non-contactable individual who described him/herself as an asthma patient, complained about a peak flow diary produced by GlaxoSmithKline UK.**

**The complainant noted the date on the peak flow diary (July 2016) and stated that it would appear that the material had not been certified in the last two years.**

**The detailed response from GlaxoSmithKline is given below.**

**The Panel noted GlaxoSmithKline's submission that the peak flow diary was originally certified in October 2016 and recertified, with no changes necessary, in October 2018. The material was not out-of-date in this regard as alleged. The Panel ruled no breaches of the Code including Clause 2.**

An anonymous, non-contactable individual who described him/herself as an asthma patient, complained about a peak flow diary (ref UK/RESP/0111a/12(2) July 2016) which he/she had been given at his/her named GP surgery. The booklet had been produced by GlaxoSmithKline UK Limited.

**COMPLAINT**

The complainant noted the date on the peak flow diary (July 2016) and stated that it would appear that the material had not been certified in the last two years. The complainant was surprised that GlaxoSmithKline did not recall out-of-date materials from GPs and alleged breaches of Clauses 2, 9.1 and 14.5 of the Code.

**RESPONSE**

GlaxoSmithKline explained that the peak flow diary was provided as a patient support item to health professionals to support adult patients monitor their peak flow pressure. The item was originally developed in July 2016 and so carried a date of preparation of July 2016; it was certified for use on 5 October 2016 in accordance with Clause 14.3 of the Code. The item was recertified on 4 October 2018 as required by Clause 14.5 but no changes to the document were required. A copy of the certificate (re-certification) was provided.

GlaxoSmithKline submitted that when materials were re-certified for continued use without any changes, it did not update the materials to amend the date of preparation. To change the date of preparation would require materials to be recalled and re-printed and use significant resources with no associated benefit to patients or health professionals.

GlaxoSmithKline stated that the GP surgery in question ordered sixty peak flow diaries directly from the company website in April 2018. There were no instructions for use of the materials.

GlaxoSmithKline stated that as the material had been re-certified for continued use at an interval of two years, it denied a breach of Clause 14.5. The company also denied breaches of Clause 9.1 for failing to maintain high standards and of Clause 2 for bringing discredit to the industry.

In response to an enquiry about the Asthma UK telephone number on the leaflet, GlaxoSmithKline stated that Asthma UK changed the number in advance of the re-approval date for the peak flow diary. However, there was a voice message referring the caller to the new number. The peak flow diary referred to a current email address.

**PANEL RULING**

The Panel noted that Clause 14.5 of the 2016 Code stated, *inter alia*, that material which was still in use must be recertified at intervals of no more than two years to ensure that it continued to conform with the relevant regulations related to advertising and the Code.

The Panel noted GlaxoSmithKline's submission that the peak flow diary was originally certified on 5 October 2016 and recertified, with no changes necessary, on 4 October 2018. The material was not out-of-date in this regard as alleged. The Panel ruled no breach of Clause 14.5 of the 2016 Code and consequently no breach of Clauses 9.1 and 2.

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|---|---|
| **Complaint received** | **20 June 2019** |
| **Case completed** | **6 September 2019** |

# CODE OF PRACTICE REVIEW – May 2020

Cases in which a breach of the Code was ruled are indexed in **bold type.**

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| **AUTH/2780/7/15** | **Anonymous employee v Astellas** | **False response and further failure to provide accurate information** | **Two breaches**<br>**Clauses 2 and 9.1** | **Appeal by respondent**<br>**Two reports from Panel to Appeal Board**<br>**Two public reprimands required by the Appeal Board**<br>**Two corrective statements required by Appeal Board**<br>**Audit required by Appeal Board**<br>**Six further re-audits required by Appeal Board**<br>**Report to ABPI Board**<br>**Suspended from membership of ABPI** | **Page 1** |
| **AUTH/2883/10/16** | **Voluntary admission by Astellas UK** | **Patient support programmes** | **Two breaches Clause 2**<br>**Breaches Clauses 7.2 and 7.9**<br>**Three breaches Clauses 9.1**<br>**Breaches Clauses 14.3, 14.5, 21 and 24.1** | **No appeal**<br>**Report from Panel to Appeal Board**<br>**Public reprimand required by Appeal Board**<br>**Audit required by Appeal Board**<br>**Three further re-audits required by Appeal Board**<br>**Report to ABPI Board**<br>**Suspended from membership of ABPI** | **Page 34** |
| **AUTH/2935/2/17** | **Anonymous ex-employee v Sunovion** | **Promotion of Latuda** | **Breaches Clauses 15.2 and 15.9** | **No appeal**<br>**Public reprimand required by Appeal Board**<br>**Audit required by Appeal Board**<br>**Two further re-audits required by Appeal Board** | **Page 51** |

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| **AUTH/2939/2/17 and AUTH/2940/2/17** | **Voluntary admission by Astellas UK and Astellas Europe** | **Failure to provide accurate prescribing information** | **Breaches Clauses 2, 4.1 (multiple), 9.1** | **No appeal**<br>**Report from Panel to Appeal Board**<br>**Public reprimand required by Appeal Board**<br>**Audit required by Appeal Board**<br>**Two further re-audits required by Appeal Board**<br>**Report to ABPI Board**<br>**Suspended from membership of ABPI** | **Page 60** |
| **AUTH/2979/9/17** | **Health professional v PharmaMar** | **Certification and promotion of Yondelis** | **Two breaches Clause 2**<br>**Breaches Clauses 3.2, 7.2 and 7.4**<br>**Two breaches Clause 9.1**<br>**Breaches Clause 12.1 and 14.1**<br>**Panel suspended use of material in accordance with Paragraph 7.1 of the Constitution and Procedure** | **No appeal**<br>**Report from Panel to Appeal Board**<br>**Public reprimand required by Appeal Board**<br>**Corrective statement required by Appeal Board**<br>**Audit required by Appeal Board**<br>**Re-audit required by Appeal Board** | **Page 73** |
| **AUTH/3013/1/18** | **AstraZeneca employee v AstraZeneca** | **Global training and advisory board and provision of incomplete and inaccurate information** | **Breaches Clauses 9.1 and 14.2** | **No appeal**<br>**Public reprimand required by Appeal Board** | **Page 82** |
| **AUTH/3027/3/18** | **Voluntary admission by Sunovion** | **Disclosure of funding to a patient organisation and provision of inaccurate information** | **Breaches Clauses 2 and 27.7** | **No appeal**<br>**Public reprimand required by Appeal Board**<br>**Audit required by Appeal Board** | **Page 100** |
| **AUTH/3031/4/18** | **Anonymous, non-contactable health professional v Gilead** | **Speaker training meeting** | **Breaches Clauses 3.2, 7.2 and 9.1** | **No appeal** | **Page 106** |

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| AUTH/3043/6/18 | Anonymous contactable v Novartis | Failure to publish joint working executive summary | No breach | Appeal by respondent | Page 120 |
| **AUTH/3044/6/18** | **Anonymous contactable v Roche** | **Failure to publish joint working executive summary** | **Breaches Clauses 9.1 and 20** | **No appeal** | **Page 130** |
| AUTH/3045/6/18 | Anonymous contactable v Pfizer | Failure to publish joint working executive summary | No breach | Appeal by respondent | Page 135 |
| AUTH/3046/6/18 | Anonymous contactable v AstraZeneca | Failure to publish joint working executive summary | No breach | Appeal by respondent | Page 148 |
| **AUTH/3053/7/18** | **Anonymous doctor v Daiichi-Sankyo** | **Speaker travel arrangements** | **Breaches Clauses 9.1 and 22.1** | **Appeal by complainant** | **Page 157** |
| **AUTH/3064/9/18** | **Gilead v ViiV Healthcare** | **Promotion of Juluca** | **Eleven breaches of Clauses 7.2, 7.3 and 7.4**<br>**Four breaches Clauses 7.9**<br>**Breach Clause 9.1** | **No appeal** | **Page 163** |
| **AUTH/3067/9/18** | **Member of the public v Chiesi** | **Payments to health professional and certification** | **Breach Clause 9.1** | **No appeal** | **Page 180** |
| **AUTH/3109/10/18** | **Anonymous v AstraZeneca** | **AstraZeneca website** | **Breaches Clauses 7.2 and 7.3**<br>**Three breaches Clause 9.1** | **No appeal** | **Page 185** |
| **AUTH/3112/11/18** | **Complainant v Lilly** | **Rheumatology website** | **Breach Clause 9.1** | **No appeal** | **Page 193** |
| **AUTH/3128/12/18** | **Complaint v Janssen** | **Promotion of Imbruvica** | **Breaches Clauses 7.2, 7.4 and 9.1** | **No appeal** | **Page 197** |
| **AUTH/3130/12/18** | **Anonymous v GlaxoSmithKline** | **Arrangements for a meeting and alleged use of LinkedIn to promote a medicine** | **Breaches Clauses 9.1, 26.1 and 26.2** | **No appeal** | **Page 201** |
| **AUTH/3133/12/18** | **Anonymous, non-contactable health professional v Novo Nordisk** | **Declaration of sponsorship of a meeting** | **Breaches Clauses 9.1, 9.10 and 22.4** | **No appeal** | **Page 210** |
| **AUTH/3138/12/18** | **Ex-employee v Indivior** | **Non-disclosure of transfers of value** | **Breaches Clauses 2, 9.1, 24.1 and 24.4** | **No appeal** | **Page 213** |
| **AUTH/3148/1/19** | **Complainant v GlaxoSmithKline** | **Online promotion of Seretide** | **Breach Clause 4.3** | **No appeal** | **Page 216** |

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| **AUTH/3151/1/19** | **Anonymous employees v Otsuka Europe** | **SPC changes and prescribing information** | **Breach Clause 2**<br>**Three breaches Clause 9.1** | **Appeal by complainants** | **Page 219** |
| **AUTH/3153/1/19** | **Anonymous, non-contactable v Otsuka UK** | **Out-of-date promotional materials** | **Breach Clause 2**<br>**Two breaches Clause 9.1 and 14.1** | **No appeal** | **Page 230** |
| **AUTH/3154/2/19** | **Complainant v Dr Falk** | **Provision of obligatory information on a website** | **Breach Clause 4.1 and 9.1** | **No appeal** | **Page 235** |
| **AUTH/3155/2/19 and AUTH/3156/2/19** | **Complainant v Bristol-Myers Squibb and Pfizer** | **Eliquis website** | **Breaches Clause 7.2 and 9.1** | **No appeal** | **Page 238** |
| **AUTH/3157/2/19** | **Voluntary admission by AstraZeneca** | **Substantiation of a claim for Fluenz Tetra** | **Breaches Clauses 7.2, 7.4 and 9.1** | **No appeal** | **Page 241** |
| AUTH/3158/2/19 | Employee v Servier | Arrangements for an advisory board | No breach | No appeal | Page 243 |
| **AUTH/3161/2/19** | **Employee v Leo** | **Alleged promotional practices** | **Breach Clause 15.9** | **No appeal** | **Page 253** |
| AUTH/3162/2/19 | Complainant v AstraZeneca | Use of Twitter | No breach | No appeal | Page 260 |
| AUTH/3164/2/19 | Complainant v Merck Sharp & Dohme | Alleged frequent and disguised promotional emails | No breach | No appeal | Page 263 |
| AUTH/3165/2/19 | Gilead Sciences v ViiV Healthcare | Promotion of Tivicay and Juluca | No breach | No appeal | Page 266 |
| **AUTH/3166/2/19** | **Complainant v Sanofi** | **Alleged promotion of Epilim on Twitter** | **Breaches Clauses 9.1, 14.5, 26.1 and 26.2** | **No appeal** | **Page 279** |
| AUTH/3167/2/19 | Complainant v Novartis | Use of Twitter/ alleged breach of undertaking | No breach | No appeal | Page 284 |
| **AUTH/3168/2/19** | **Complainant v Janssen** | **Company website** | **Breaches Clauses 4.6, 7.2, 7.9**<br>**Three breaches Clause 9.1** | **No appeal** | **Page 292** |
| **AUTH/3169/3/19** | **Voluntary admission by Otsuka Europe** | **Revision of Jinarc SPC** | **Breach Clause 2**<br>**Two breaches Clause 9.1**<br>**Breach Clause 29** | **No appeal** | **Page 300** |
| AUTH/3170/3/19 | Health professional v Novartis | Presentation at speaker meeting | No breach | No appeal | Page 305 |

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| AUTH/3171/3/19 | Anonymous contactable health professional v Novartis | Provision of a meeting certificate | No breach | No appeal | Page 308 |
| AUTH/3172/3/19 | Anonymous v Sandoz | Conduct of a representative | No breach | No appeal | Page 311 |
| **AUTH/3174/3/19** | **Anonymous employees v Otsuka Europe** | **Conduct of Otsuka Europe** | **Two breaches Clause 2**<br>**Two breaches Clause 9.1**<br>**Breach Clause 12.1** | **Appeal by complainants** | **Page 316** |
| **AUTH/3176/3/19** | **Complainant v Orion Pharma** | **Email and website** | **Two breaches 9.1 and 9.10** | **No appeal** | **Page 325** |
| **AUTH/3177/3/19** | **Complainant v Grünenthal** | **Promotional use of LinkedIn** | **Breaches Clauses 4.1, 4.3, 4.9, 9.1, 9.9, 14.1, 26.1, 26.2 and 28.1** | **No appeal** | **Page 329** |
| **AUTH/3180/4/19** | **Respiratory nurse v AstraZeneca** | **Material on a personal social media account** | **Breaches Clauses 9.1 and 15.2** | **No appeal** | **Page 334** |
| **AUTH/3182/4/19** | **Pharmacist v Astellas** | **Frequency of telephone calls by representatives** | **Breaches Clauses 15.2 and 15.4** | **No appeal** | **Page 340** |
| AUTH/3186/5/19 | Anonymous, non-contactable v Almirall | Arrangements for a meeting | No breach | No appeal | Page 344 |
| AUTH/3187/5/19 | Anonymous, non-contactable representative v Cipla | Conduct of a senior manager | No breach | No appeal | Page 349 |
| **AUTH/3205/6/19** | **Voluntary admission by Boehringer Ingelheim** | **Lack of certification and obligatory information** | **Breaches Clauses 4.1, 4.3, 4.8, 4.9**<br>**Two breaches Clause 14.1** | **No appeal** | **Page 353** |
| **AUTH/3208/6/19** | **Member of the public v Merz** | **Alleged promotion on Instagram** | **Breaches Clauses 9.1, 15.2 and 26.1** | **No appeal** | **Page 357** |
| AUTH/3210/6/19 | Patient v GlaxoSmithKline | Alleged out-of-date patient material | No breach | No appeal | Page 362 |

# PMCPA | Prescription Medicines Code of Practice Authority

The Prescription Medicines Code of Practice Authority was established by the Association of the British Pharmaceutical Industry (ABPI) in 1993 to operate the Code of Practice for the Pharmaceutical Industry at arm's length from the ABPI itself. Compliance with the Code is obligatory for ABPI member companies and, in addition, over sixty non member companies have voluntarily agreed to comply with the Code and to accept the jurisdiction of the Authority.

The Code covers the advertising of medicines to health professionals and other relevant decision makers and also covers information about prescription only medicines made available to the public.

It covers:

- journal and direct mail advertising
- the activities of representatives, including any printed or electronic material used by them
- the supply of samples
- the provision of inducements in connection with the promotion of medicines and inducements to prescribe, supply, administer, recommend, buy or sell medicines by the gift, offer or promise of any benefit or bonus, whether in money or in kind
- the provision of hospitality
- the organisation of promotional meetings
- the sponsorship of scientific and other meetings, including payment of travelling and accommodation expenses
- the sponsorship of attendance at meetings organised by third parties
- all other sales promotion in whatever form, such as participation in exhibitions, the use of audio or video-recordings in any format, broadcast media, non-print media, the Internet, interactive data systems, social media and the like.

It also covers:

- the provision of information on prescription only medicines to the public either directly or indirectly, including by means of the Internet
- relationships with patient organisations
- disclosure of tranfers of value to health professionals and organisations
- joint working between the NHS and pharmaceutical companies
- the use of consultants
- non-interventional studies of marketed medicines
- the provision of items for patients
- the provision of medical and educational goods and services
- grants, donations and benefits in kind to institutions.

Complaints submitted under the Code are considered by the Code of Practice Panel which consists of three of the four members of the Code of Practice Authority acting with the assistance of independent expert advisers where appropriate. One member of the Panel acts as case preparation manager for a particular case and that member does not participate and is not present when the Panel considers it.

Both complainants and respondents may appeal to the Code of Practice Appeal Board against rulings made by the Panel. The Code of Practice Appeal Board is chaired by an independent legally qualified Chairman, Mr William Harbage QC, and includes independent members from outside the industry. Independent members, including the Chairman, must be in a majority when matters are considered by the Appeal Board.

In each case where a breach of the Code is ruled, the company concerned must give an undertaking that the practice in question has ceased forthwith and that all possible steps have been taken to avoid a similar breach in the future. An undertaking must be accompanied by details of the action taken to implement the ruling. Additional sanctions are imposed in serious cases.

Further information about the Authority and the Code can be found at www.pmcpa.org.uk

Complaints under the Code should be sent to the Director of the Prescription Medicines Code of Practice Authority, 7th Floor, Southside, 105 Victoria St, London SW1E 6QT

telephone 020 7747 8880
by email to: complaints@pmcpa.org.uk.