NUMBER 79 February 2013

CODE OF PRACTICE REVIEW

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 ABPI Code of Practice for the Pharmaceutical Industry independently of the Association itself.

ETHICAL STANDARDS IN HEALTH AND LIFE SCIENCES GROUP CONSULTATION ON PAYMENTS TO HEALTHCARE PROFESSIONALS

The Ethical Standards in Health and Life Sciences Group (ESHLSG), the multi stakeholder group of healthcare organisations, is currently running a survey to look at the public disclosure of payments to healthcare professionals. The consultation is intended to establish whether there is support in principle for a system of public declaration of payments. The survey together with further details about the group's membership and its activities can be found at eshlsg.org.

MHRA ANNUAL MEETING AND REPORT

The Medicines and Healthcare products Regulatory Agency has published its annual report for 2012. There were fewer than ten complaints about prescription medicines, four cases were upheld of which three cases concerned advertising by companies holding manufacturing licences but not marketing authorizations for the products (specials manufacturers). The long term downward trend in the number of advertising cases in this sector continued in 2012. The MHRA will continue to work proactively with self regulatory bodies and others to maintain high standards. At its annual meeting the MHRA strongly supported self regulation which had been shown time and again to be effective.

NEW INDEPENDENT MEMBERS OF THE APPEAL BOARD

Mrs Gillian Hawken and Dr Howard Freeman have recently been appointed to the Code of Practice Appeal Board as independent members. Both are welcomed by the Authority. Mrs Hawken is a solicitor with her own practice and joins as the lay member.

Dr Freeman joins as a medical member. He is the senior partner in a GP practice and has worked in a number of senior NHS management roles, most recently as Associate Medical Director at the London Strategic Health Authority.

PUBLIC REPRIMAND FOR CHIESI

Chiesi Limited has been publicly reprimanded by the Code of Practice Appeal Board for failing to provide the Code of Practice Panel with complete and accurate information at the outset in response to a complaint (Case AUTH/2435/8/11).

In 2011 the Panel ruled breaches of the Code in relation to the promotion of Fostair (beclomethasone and formoterol) for an unlicensed indication. In order to make its rulings, however, the Panel had to repeatedly ask Chiesi for further information. Chiesi's submission in this case was inconsistent with its submission in a previous similar case.

The Panel reported Chiesi to the Appeal Board. On consideration of that report in December 2011, the Appeal Board considered that it was vital that responses to the Authority were comprehensive and not misleading. Chiesi's failure to provide complete and accurate information was unacceptable. The Appeal Board required an audit of Chiesi's procedures in relation to the Code and a subsequent re-audit.

The first audit was conducted in March 2012 and upon consideration of the second audit report in November 2012 the Appeal Board noted that progress had been made but requested that the Authority review the company's revised standard operating procedures (SOPs). Following the Authority's assessment of the SOPs, the Appeal Board decided in January 2013 that sufficient progress had been made and on the basis that this was maintained, no further action was required.

Full details of Case AUTH/2435/8/11 can be found at page 15 of this issue of the Review.

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 seminars comprise a full day course offering 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.

The next Code of Practice seminar dates on which places remain available are:

Friday, 10 May
Tuesday, 23 July

Short training sessions on the Code or full all 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
Facsimile: 020 7747 8881

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.
Heather Simmonds: 020 7747 1438
Etta Logan: 020 7747 1405
Jane Landles: 020 7747 1415

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.

PROPOSED AMENDMENT TO THE SECOND 2012 EDITION

The PMCPA recently published proposals to amend the requirements in the Code regarding the ABPI examinations for representatives. The proposals remove the requirement to take the ABPI examinations exclusively. The ABPI has been the sole provider of a qualification for representatives for many years but has recently been made aware that a company is hoping to launch an alternative qualification. Full details of the proposed amendments can be found on the PMCPA website.

CLINICAL TRIAL TRANSPARENCY

The ABPI has announced that it will be appointing an independent, third party service provider to monitor compliance with the clinical trial transparency provisions in Clause 21.3 of the Code. The ABPI is also developing a toolkit to provide good practice guidelines, checklists and template standard operating procedures.

CASE AUTH/2411/6/11

PHARMACOSMOS v VIFOR

Ferinject video

Pharmacosmos A/S complained about a video issued by Vifor Pharma UK which referred to Ferinject (ferric carboxymaltose) solution for injection/infusion. Ferinject was indicated for the treatment of iron deficiency when oral iron preparations were ineffective or could not be used.

Pharmacosmos understood that Vifor agreed with the NHS Alliance to contribute to NHS Alliance TV news, an hour-long video which was to be shown at the NHS Alliance conference and posted on the NHS Alliance website. The theme of the conference was to focus on the Quality, Innovation, Productivity and Prevention (QIPP) initiative. The title of the video was 'Delivering QIPP by redesigning iron services'. Vifor provided speakers and allowed filming at its premises. The script was reviewed internally and the video was signed off according to Vifor's procedures.

Pharmacosmos stated that Vifor did not regard its involvement in the video or its content as being promotional and this was at the crux of this case.

Pharmacosmos stated that its complaint was about the video being made available to health professionals in the first place as part of the NHS Alliance conference. Pharmacosmos alleged that it was not clear to the intended audience that the video constituted a promotional presentation from Vifor, in breach of the Code.

The claim 'for patients it would mean a speedier recovery' appeared immediately following a statement that 'Iron treatment protocols are placing a burden on the NHS'. Taken in context with later comments in the video about Ferinject, the clear inference was that Ferinject could speed recovery by allowing the iron services to be redesigned, which was misleading, in breach of the Code.

The first time the brand name was used meant that the generic name and an indication that the product was under intensive monitoring from the Committee on the Safety of Medicine (CSM) was needed. In the absence of a visual indication on screen, this should be stated in the commentary. In addition, the failure to provide prescribing information was in breach of the Code.

Pharmacosmos alleged that the claim 'Ferinject provides ... all the iron they need in just one 30 minute visit' was misleading as not all patients treated with Ferinject could be given all the iron they needed in a single infusion. The maximum dose of Ferinject per treatment was 1000mg and 15mg/kg.

Pharmacosmos stated that it had serious concerns about Vifor's approach to the project as exhibited in the inter-company dialogue. The combined effect of disguised promotion, misleading claims and missing obligatory information constituted a considerable failure to maintain controls and standards.
The detailed response from Vifor is given below.

The Panel noted that the video opened with a sequence which featured the Vifor company name and logo in the centre of the screen together with the title 'Delivering QIPP by redesigning iron services'. In this regard the Panel considered that there was no doubt that the video had been sponsored by Vifor; the company's involvement was clear from the outset. No breach of the Code was ruled.

The Panel considered that although the title of the video was not product related its content was such that most viewers would consider that it promoted Ferinject. The first two minutes of the 3:44 minute video were about general issues but then the information was specifically about Ferinject. The Panel considered that the video was clearly promotional and in that regard its nature was not disguised. No breach of the Code was ruled.

The Panel noted that the video had been filmed at Vifor's offices, Vifor had suggested speakers; its general manager had spoken on the video. The draft script had been reviewed internally and signed off according to company procedure. Vifor had submitted that its input into the video stopped at this stage. The Panel noted that a document provided by Vifor, entitled 'Story Outline', appeared to be a written agreement between the NHS Alliance, the film company and Vifor. The document listed three key messages: 'Vifor Pharma want to raise awareness of their product, Ferinject'; 'Vifor Pharma want to raise awareness of iron deficiency, its symptoms, how anaemia could be better treated now and for patients in the future' and 'Vifor Pharma want to start a conversation among doctors about how this illness is best treated and help them discuss the best funding options with the NHS'. In the Panel's view there was thus no doubt that, at the outset and contrary to the company's response, Vifor knew that the video would promote Ferinject; to consider otherwise demonstrated a fundamental lack of understanding of the Code and its requirements. In this regard the Panel noted the definition of promotion was any activity undertaken by a pharmaceutical company or with its authority which promoted the prescription, supply, sale or administration of its medicines. The Panel considered that Vifor's submission that its intention was simply to help the debate around the practicality of QIPP by giving a practical example was disingenuous. The Panel considered that the video should have contained prescribing information and other obligatory information for Ferinject which it did not. A breach of the Code was ruled.

In relation to the claim 'for patients it would mean a speedier recovery' the Panel noted that this appeared in a section referring to changes to intravenous (IV) iron services design which would deliver valuable QIPP outcomes. For patients it would mean a speedier recovery and fewer visits to hospital. The previous section referred to Ferinject as the perfect solution to the usual treatment which involved numerous trips to hospital for iron injections over a long period of time. Where Ferinject could be administered as a single dose infusion, the treatment course was shorter than that for products that needed multiple visits. However there was another medicine, Cosmofer (iron (III)-hydroxide dextran complex) which could be administered as a single dose albeit over a longer time period compared to Ferinject. Contrary to Vifor's submission the Panel considered that the claim implied that Ferinject would speed recovery. This was not always so. The Panel did not consider that redesigning the service to use Ferinject would mean a speedier recovery. The Panel considered that the claim was misleading and a breach of the Code was ruled.

In relation to the allegation about the claim 'Ferinject provides … all the iron they need in just one 30 minute visit', the Panel noted that the claim in the video was not the same. The video stated 'Iron deficiency is currently treated either by a long day in hospital, or multiple visits. But … Ferinject is different. The patient can receive all the IV iron they need in just one thirty minute visit'. Although the Panel had concerns that, in effect, the claim in the video implied that Ferinject provided all the iron needed in just one visit (as noted above) and that was not so, there was no actual claim that Ferinject provided all the iron needed in just one 30 minute visit as alleged. Nevertheless, the Panel ruled that the implication of the claim in the video was misleading in breach of the Code.

Overall, the Panel found it difficult to understand how the video could be seen as anything other than promotional. The Panel considered that Vifor's conduct in relation to the Code warranted consideration by the Code of Practice Appeal Board and it decided to report the company to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to consider whether further sanctions were warranted.

The Appeal Board was extremely concerned that Vifor had considered the video non-promotional and in that regard it referred in particular to the key message in 'Story Outline', 'Vifor Pharma want to raise awareness of their product, Ferinject'. The Appeal Board noted Vifor's submission that it had not intended to promote its product. Promotion was defined in the Code as 'any activity undertaken by a pharmaceutical company …. which promotes the prescription, supply, sale or administration of its medicines'. The Appeal Board noted that a company's intention was not relevant when considering whether its materials or activities were promotional. In the Appeal Board's view the video and the story outline were clearly promotional in nature. The Appeal Board was also extremely concerned about some of the claims made in the video and queried whether they complied with the Code. In the Appeal Board's view, the fact that the video had been certified through the copy approval system compounded the errors within.

The Appeal Board considered that Vifor's actions demonstrated a fundamental lack of understanding of the Code and its requirements. This case raised very serious concerns regarding the expertise of Vifor's signatories and the role of senior management in compliance matters.

The Appeal Board noted that Vifor had accepted that it had made serious errors and in that regard had already started a review of its policies and procedures. Nonetheless, the Appeal Board decided that Vifor's procedures in relation to the Code should be audited as soon as possible by the Authority. On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary.

The Appeal Board was also extremely concerned that the video might still be in use by some third parties and so it decided to require Vifor to take immediate steps to recover the video by writing to each recipient to ask them, where practical, to return it. The letter should explain why such action was necessary.

Upon receipt of a letter from Vifor regarding the recovery of the video the Appeal Board noted that the NHS Alliance had sent 990 DVDs, which included the Vifor film, to staff in primary care trusts, foundation trusts, acute trusts, local authorities and central government departmental bodies and agencies. The Appeal Board decided that in the circumstances Vifor should work with the NHS Alliance to ensure that those who had been sent copies of the DVD be informed that Vifor's contribution, following a complaint under the Code, had been ruled in breach of the Code and that full details could be found on the PMCPA website.

Vifor was first audited in November 2011 and upon receipt of that audit report the Appeal Board was concerned that the audit report indicated that Vifor had much work to do. It noted from Vifor's response that a preliminary corrective and preventative actions programme had been drawn up. It requested that Vifor be asked to provide timescales. It also decided that Vifor should be asked to provide copies of the correspondence between the company and its head office about the audit report and details about the role of an external consultant.

The Appeal Board was concerned to note that since deciding that Vifor should be audited, another case, which involved a breach of undertaking (Case AUTH/2442/10/11), had been considered by the Panel. On the day of the audit that case was still on going and so was not discussed. The Appeal Board noted, however, that the case had now completed.

The Appeal Board decided that Vifor should be re-audited in March 2012. On receipt of the report for that audit, the Appeal Board would consider if further sanctions were necessary.

Upon receipt of the March 2012 audit report the Appeal Board was disappointed at the lack of progress since the November 2011 audit particularly with regard to the revision of standard operating procedures (SOPs). The Appeal Board noted that new staff were due to be appointed. The Appeal Board considered that Vifor should be re-audited in six months time at which point it expected there to be significant improvement. In the meantime Vifor should provide by the end of June a detailed interim response to the recommendations of the March 2012 audit to include an update on recruitment and SOPs. If the Appeal Board was not satisfied then the re-audit would be brought forward.

Upon receipt of the next audit report, the Appeal Board would decide whether further sanctions were necessary.

On consideration of the interim response from Vifor, the Appeal Board decided that there was no need to reaudit sooner than the currently arranged date, in October 2012.

Upon receipt of the October audit report, the Appeal Board noted that good progress had been made since the last audit. New staff had been appointed who would have key roles in compliance. New standard operating procedures had been written and resources had been committed to Code compliance. The Appeal Board considered that on the basis that Vifor's current commitment to compliance was maintained, no further action was required.

Pharmacosmos A/S complained about a video issued by Vifor Pharma UK Limited which referred to Ferinject (ferric carboxymaltose) solution for injection/infusion. Ferinject was indicated for the treatment of iron deficiency when oral iron preparations were ineffective or could not be used.

COMPLAINT

Pharmacosmos understood from inter-company dialogue that Vifor agreed with the NHS Alliance to contribute to NHS Alliance TV news, an hour-long video which was to be shown at the NHS Alliance conference and posted on the NHS Alliance website. The theme of the conference was to focus on the Quality, Innovation, Productivity and Prevention (QIPP) initiative. The title of the video was 'Delivering QIPP by redesigning iron services'. Pharmacosmos stated that as Vifor entered into this video as partners with the NHS Alliance it was responsible for the content under Clauses 1.2 and 1.8 of the Code. Vifor's view was that perceived benefits of Ferinject aligned with the principles of QIPP and explained these in the video. However, Vifor did not regard its involvement in the video or its content as being promotional. This difference in opinion was at the crux of this case.

Vifor provided speakers and allowed filming at its premises. Vifor stated that the script was reviewed internally and the video was signed off according to Vifor's internal procedures (Pharmacosmos was not sure if it was certified).

Subsequently, Vifor was approached by a third party media company to host the video on its website and gave its permission. The third party media company subsequently emailed registered users of the website (whom Pharmacosmos believed to be both heath professionals and members of the public) about new information on the website. As such, the company had acted on behalf of Vifor (and the NHS Alliance) and so Vifor was responsible for the actions of the agency. In inter-company dialogue Vifor had categorically denied responsibility for this email. Pharmacosmos understood that the email had been sent to a wide group of UK health professionals. Pharmacosmos alleged that the content and nature of the email was promotional and within the scope of the Code. It was clear that Vifor did not conduct any meaningful checks on the nature of the third party media company or control the availability of the video and after Pharmacosmos brought the matter to Vifor's attention, Vifor realised that the media company was not part of the NHS Alliance and arranged for the video to be removed from the website. The email was sent in April.

Pharmacosmos stated that it was not at this time raising specific concerns in relation to the email's content or its distribution. Nor was it currently raising any formal complaint in respect of the placement of the video on the website. However it wished to consider the email and the interactions with the third party media company as part of Vifor's overall approach to this project.

Vifor had clearly stated that the video was shown at the NHS Alliance conference and that it gave permission for the video to be displayed on a freely accessible website and that attention was drawn to the video by an email. The video was thus clearly distributed and viewed by a number of different audiences. Pharmacosmos did not believe that withdrawing the video from the third party website was an appropriate response as this action was only in relation to the perceived risk of promoting to the general public, a matter about which it was not complaining.

Pharmacosmos stated that its complaint was about the video being made available to health professionals in the first place as part of the NHS Alliance conference.

As clearly stated in inter-company correspondence, Vifor appeared to believe that its actions were both compliant and responsible. It had completely misunderstood the Code in respect of the fundamental activity, which was that it knowingly participated in creating and distributing a promotional video without sufficient controls or declarations. This raised serious concerns about Vifor's understanding of the Code.

Transparency: Pharmacosmos alleged that it was not clear to the intended audience that the video constituted a promotional presentation from Vifor (as partners in the production), in breach of Clauses 12.1 and 9.10. The video was created in the form of a news report, which added to the impression that it was non-promotional.

However the video clearly promoted the virtues of Ferinject.

Claim, 'for patients it would mean a speedier recovery': This claim appeared immediately following a statement that: 'Iron treatment protocols are placing a burden on the NHS'. Taken in context with the comments that followed later in the video regarding Ferinject specifically, the clear inference was that Ferinject could speed recovery by allowing the iron services to be redesigned, which was misleading, in breach of Clause 7.2.

Obligatory information: The first time the brand name was used meant that the generic name and an indication that the product was under intensive monitoring from the Committee on the Safety of Medicine (CSM) was needed. In the absence of a visual indication on screen, this should be stated in the commentary. A breach of Clause 4.3 was alleged.

In addition, Pharmacosmos alleged that the failure to provide prescribing information was in breach of Clause 4.1.

Claim, 'Ferinject provides....all the iron they need in just one 30 minute visit': Not all patients treated with Ferinject could be given all the iron they needed in a single infusion. The maximum dose of Ferinject per treatment was 1000mg and 15mg/kg. Pharmacosmos alleged that the claim was misleading in breach of Clause 7.2. Pharmacosmos submitted that it was for Vifor to prove why Ferinject provided 'all the iron they needed', not for Pharmacosmos to disprove it.

Overall, Pharmacosmos stated that it had serious concerns about Vifor's approach to the project as exhibited in the inter-company dialogue. The combined effect of disguised promotion, misleading claims and missing obligatory information constituted a considerable failure to maintain controls and standards.

RESPONSE

Vifor stated that the QIPP initiative was driven at a national, regional and local level to support clinical teams and NHS organisations to improve the quality of care they delivered while making efficiency savings that could be reinvested in the service to deliver year on year quality improvements.

The NHS Alliance, organisers of the November 2010 NHS Alliance Annual Conference, asked Vifor to contribute to the 'NHS Alliance TV News', an hour long video, which was to be shown at the meeting. The conference theme was to focus on QIPP and the NHS Alliance proposed that redesigning iron services would be an appropriate example to highlight the financial and patient benefits of QIPP initiatives. The topics were agreed and a contract signed with the story title of 'Delivering QIPP by redesigning iron services'. A copy of the transcript was provided.

Vifor stated that the NHS Alliance considered Vifor might be able to help with this project, as for the vast majority of patients currently needing intravenous (IV) iron five hospital visits were required to administer 1g of Venofer (a Vifor Pharma product) in the form of 200mg per visit. With Ferinject, these patients could be given 1g in one 30 minute visit, bringing about benefits consistent with the QIPP programme.

At the request of the NHS Alliance, Vifor suggested speakers and allowed filming at its premises and production was carried out by a film company on behalf of the NHS Alliance. The draft script was reviewed internally and signed off according to Vifor's internal procedures. The company's input into the video stopped at this stage.

As the video concentrated not on the product but on the QIPP service delivery benefits, the video was regarded as non-promotional. There was no intention to promote Ferinject and so Vifor did not include the prescribing information.

The video featured two independent speakers each with a broad experience in IV iron management; a clinician with expertise in clinical research with IV iron and a nurse who ran an anaemia clinic in a teaching hospital. The content was controlled entirely by the NHS Alliance and it had the final say over its content.

Vifor explained that the NHS Alliance brought together GP consortia, primary care trusts, clinicians and managers in primary care. Over 850 clinicians and managers attended the 2010 NHS Alliance Annual Conference to debate the implications of the Government's reforms and to learn from leading innovators in commissioning and the provision of integrated care. The video was over 2 minutes long and was played along with other videos, each loop lasting over an hour. Vifor had no stand; it was a specialist company which concentrated on secondary care products and did not promote in primary care.

There was no intention to promote and under the circumstances it could be clearly seen that there was no intention for disguised promotion and so no breach of Clause 12.1. Sponsorship was very clear in the video so this was not a breach of Clause 9.10.

Taken in context, one visit for 1g of iron vs five visits each of 200mg of iron given over several weeks clearly was a treatment given in a shorter time for the condition in question. This was therefore not in breach of Clause 7.2 as the statement did not imply that Ferinject could speed recovery.

The video was over 2 minutes in an hour long video presentation to highlight QIPP benefits. Vifor entered into an agreement with the NHS Alliance which had complete control over the video and Vifor's intention was simply to help the debate around the practicality of QIPP by giving a practical example. As this was service-focused and non-promotional the prescribing information was not added.

In line with its summary of product characteristics (SPC), Ferinject could be given in 15 minutes for 1g

of IV iron; the statement in the video was intended to reflect current clinical practice and had included the set up time as well in the 30 minutes quoted. This obviously compared favourably to five visits for Venofer thus achieving the required iron replenishment in 30 minutes. This was not misleading and thus not in breach of Clause 7.2.

Vifor submitted that when, in late April 2011, it realised that the third party media company was not affiliated to the NHS Alliance, it asked for the video to be removed from the website immediately. Vifor stated that it had been ruled in breach of this already [Case AUTH/2399/4/11] and it had fully acknowledged its mistake in this respect.

In response to a request for further information Vifor stated that it paid for the production of its item on the video along with other organisations that took part in the video. The payment was 50% of the actual cost for the partnership.

PANEL RULING

The Panel noted that although Pharmacosmos had raised a number of concerns about the video and its distribution to various audiences, the complaint was limited to the video being made available to health professionals at the 2010 NHS Alliance Annual Conference.

The Panel noted that the video opened with a sequence which featured the Vifor company name and logo in the centre of the screen together with the title 'Delivering QIPP by redesigning iron services'. In this regard the Panel considered that there was no doubt that the video had been sponsored by Vifor; the company's involvement was clear from the outset. No breach of Clause 9.10 was ruled.

The Panel considered that although the title of the video was not product related ('Delivering QIPP by redesigning iron services') its content was such that most viewers would consider that it promoted Ferinject. The first two minutes of the 3:44 minute video were about general issues but between the second and third minutes all of the information was specifically about Ferinject. The Panel considered that the video was clearly promotional and in that regard its nature was not disguised. No breach of Clause 12.1 was ruled.

The Panel noted that the video had been filmed at Vifor's offices, Vifor had suggested speakers; its general manager had spoken on the video. The draft script had been reviewed internally and signed off according to company procedure. Vifor had submitted that its input into the video stopped at this stage. The Panel noted that a document provided by Vifor, entitled 'Story Outline', appeared to be a written agreement between the NHS Alliance, the film company and Vifor. The document listed three key messages one of which was 'Vifor Pharma want to raise awareness of their product, Ferinject'. The others being 'Vifor Pharma want to raise awareness of iron deficiency, its symptoms, how anaemia could be better treated now and for patients in the future' and 'Vifor Pharma want to start a conversation among doctors about how this illness is best treated and help them discuss the best funding options with the NHS'. In the Panel's view there was thus no doubt that, at the outset and contrary to the company's response, Vifor knew that the video would promote Ferinject; to consider otherwise demonstrated a fundamental lack of understanding of the Code and its requirements. In this regard the Panel noted the definition of promotion in Clause 1.2 was any activity undertaken by a pharmaceutical company or with its authority which promoted the prescription, supply, sale or administration of its medicines. The Panel considered that Vifor's submission that its intention was simply to help the debate around the practicality of QIPP by giving a practical example was disingenuous. The Panel considered that the video should have contained prescribing information and other obligatory information for Ferinject which it did not. A breach of Clauses 4.1 and 4.3 was ruled.

In relation to the claim 'for patients it would mean a speedier recovery' the Panel noted that this appeared in a section referring to changes to IV iron services design which would deliver highly valuable QIPP outcomes. For patients it would mean a speedier recovery and fewer visits to hospital. The previous section referred to Ferinject as the perfect solution to the usual treatment which involved numerous trips to hospital for iron injections over a long period of time. Where Ferinject could be administered as a single dose infusion, the treatment course was shorter than that for products that needed multiple visits. However there was another medicine, Cosmofer (iron (III)-hydroxide dextran complex) which could be administered as a single dose albeit over a longer time period (4-6 hours) compared to Ferinject (30 minutes including the set up time). Contrary to Vifor's submission the Panel considered that the claim implied that Ferinject would speed recovery. This was not always so. According to its SPC the IV infusion was up to a maximum single dose of 20ml of Ferinject (1000mg of iron) but not exceeding 0.3ml of Ferinject (15mg of iron) per kg body weight. Ferinject 20ml was not to be administered as an infusion more than once a week. The Panel did not consider that redesigning the service to use Ferinject would mean a speedier recovery. The Panel considered that the claim was misleading and a breach of Clause 7.2 was ruled.

In relation to the allegation about the claim 'Ferinject provides … all the iron they need in just one 30 minute visit', the Panel noted that the claim in the video was not the same. The video stated 'Iron deficiency is currently treated either by a long day in hospital, or multiple visits. But … Ferinject is different. The patient can receive all the IV iron they need in just one thirty minute visit'. Although the Panel had concerns that, in effect, the claim in the video implied that Ferinject provided all the iron needed in just one visit (as noted above) and that was not so, there was no actual claim that Ferinject provided all the iron needed in just one 30 minute visit as alleged. Nevertheless, the Panel considered that the implication of the claim in the video was misleading and thus the Panel ruled a breach of Clause 7.2.

Taking all the circumstances into account the Panel found it difficult to understand how the video could be seen as anything other than promotional material. The Panel considered that Vifor's conduct in relation to the Code warranted consideration by the Code of Practice Appeal Board and it decided to report the company to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to consider whether further sanctions were warranted.

COMMENTS FROM VIFOR ON THE REPORT

Vifor's presentation during the consideration of the report also covered the report in Case AUTH/2422/7/11.

Vifor submitted that it fully accepted the gravity of the report to the Appeal Board. The company noted that the video in question was withdrawn as soon as it received the first letter of complaint from Pharmacosmos on 26 April and it had not been used since. Vifor stated that its intention was simply to support the QIPP conference but it accepted that it had not fully understood the scope of the video and it took full responsibility for its actions. Vifor submitted that it was an ethical company, committed to abiding to the letter and spirit of the Code and had started a complete review of its internal processes in order to ensure that it fully complied with the Code.

Vifor apologised and accepted that the company had made significant errors which had led to the Panel's rulings of breaches of the Code. Vifor had considered that the video was non-promotional, as the intention was not to promote the product, and it had mistakenly signed it off as such. During the consideration of the report the Vifor representatives mentioned that third parties including the ABPI had used either the video or the information. Vifor submitted that as part of its internal review of processes it had increased support for medical sign-off. Vifor noted that it had recently been inspected by the Medicines and Healthcare products Regulatory Agency (MHRA). Vifor was confident that it had robust procedures in place to ensure that previous errors were not repeated.

APPEAL BOARD CONSIDERATION

The Appeal Board was extremely concerned that Vifor had considered that the video was non-promotional and in that regard it referred in particular to the 'Story Outline' which stated that one of the key messages was 'Vifor Pharma want to raise awareness of their product, Ferinject'. The Appeal Board noted Vifor's submission that it had not intended to promote its product. Promotion was defined in Clause 1.2 of the Code as 'any activity undertaken by a pharmaceutical company …. which promotes the prescription, supply, sale or administration of its medicines'. The Appeal Board noted that a company's intention was not relevant when considering whether its materials or activities were promotional. In the Appeal Board's view the video and the story outline were clearly promotional in nature. The Appeal Board was also extremely concerned about some of the claims made in the video and queried whether they complied with the Code. In the Appeal Board's view, the fact that the video had been certified through the copy approval system compounded the errors within.

The Appeal Board considered that Vifor's actions demonstrated a fundamental lack of understanding of the Code and its requirements. This case raised very serious concerns regarding the expertise of Vifor's signatories and the role of senior management in compliance matters.

The Appeal Board noted that Vifor had accepted that it had made serious errors and in that regard had already started a review of its policies and procedures. Nonetheless, the Appeal Board decided, in accordance with Paragraph 11.3 of the Constitution and Procedure, to require an audit of Vifor's procedures in relation to the Code to be carried out by the Authority. The audit should be conducted as soon as possible. On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary.

The Appeal Board was also extremely concerned that the video might still be in use by some third parties and so it decided, in accordance with Paragraph 11.3, to require Vifor to take immediate steps to recover the video by writing to each recipient to ask them, where practical, to return it. The letter should explain why such action was necessary.

FURTHER CONSIDERATION BY THE APPEAL BOARD

Upon receipt of a letter from Vifor regarding the recovery of the video the Appeal Board noted that the NHS Alliance had sent 990 DVDs, which included the Vifor film, to staff in primary care trusts, foundation trusts, acute trusts, local authorities and central government departmental bodies and agencies. The Appeal Board decided that in the circumstances Vifor should work with the NHS Alliance to ensure that those who had been sent copies of the DVD be informed that Vifor's contribution, following a complaint under the Code, had been ruled in breach of the Code and that full details could be found on the PMCPA website.

Vifor was first audited in November 2011 and upon receipt of that audit report the Appeal Board was concerned that the report indicated that Vifor had much work to do. It noted from Vifor's response that a preliminary corrective and preventative actions programme had been drawn up. It requested that Vifor be asked to provide timescales for the actions. It also decided that Vifor should be asked to provide copies of the correspondence between the company and its head office about the audit report and details about the role of an external consultant.

The Appeal Board was concerned to note that since deciding that Vifor should be audited, another case which involved a breach of undertaking, Case AUTH/2442/10/11, had been considered by the Panel. On the day of the audit that case was still ongoing and so was not discussed. The Appeal Board noted, however, that the case had now completed.

The Appeal Board decided that Vifor should be re-audited in March 2012. On receipt of the report for

that audit, the Appeal Board would consider if further sanctions were necessary.

Upon receipt of the March 2012 audit report the Appeal Board was disappointed at the lack of progress since the November 2011 audit particularly with regard to the revision of standard operating procedures (SOPs). The Appeal Board noted that new staff were due to be appointed. The Appeal Board considered that Vifor should be re-audited in six months time at which point it expected there to be significant improvement. In the meantime Vifor should provide a detailed interim response to the recommendations of the March 2012 audit to include an update on recruitment and SOPs. This interim response should be provided by the end of June 2012 and Vifor advised that if the Appeal Board was not satisfied then the re-audit would be brought forward.

Upon receipt of the next audit report, the Appeal Board would decide whether further sanctions were necessary.

On consideration of the interim response from Vifor, the Appeal Board decided that there was no need to reaudit sooner than the currently arranged date, in October 2012.

Upon receipt of the October audit report, the Appeal Board noted that good progress had been made since the last audit. New staff had been appointed who would have key roles in compliance. New standard operating procedures had been written and resources had been committed to Code compliance. The Appeal Board considered that on the basis that Vifor's current commitment to compliance was maintained, no further action was required.

Complaint received	**22 June 2011**
Undertaking received	**17 August 2011**
Appeal Board consideration	**12 October 2011** **16 November 2011** **7 December 2011** **19 April 2012** **26 July 2012** **15 November 2012**
Interim case report first published	**23 January 2012**
Case completed	**15 November 2012**

CASE AUTH/2422/7/11

PHARMACOSMOS v VIFOR

Ferinject leavepiece

Pharmacosmos complained about a Ferinject (ferric carboxymaltose) solution for injection/infusion leavepiece issued by Vifor Pharma. Ferinject was indicated for the treatment of iron deficiency when oral preparations were ineffective or could not be used. The claims at issue were both referenced to Geisser (2009).

The detailed responses from Vifor are given below.

Pharmacosmos alleged that the claim 'Ferinject avoids dextran-induced hypersensitive reactions' was not balanced or fair because there was no mention that Ferinject itself might cause hypersensitivity reactions as stated in the Ferinject summary of product characteristics (SPC). The material was not sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine.

The Panel noted that the Ferinject SPC, stated that 'Parenterally administered iron preparations can cause hypersensitivity reactions including anaphylactoid reactions, which may be potentially fatal ...Therefore, facilities for cardio-pulmonary resuscitation must be available'. Hypersensitivity including anaphylactoid reactions was listed as an uncommon side effect. The only reference to this possible side effect to Ferinject in the leavepiece was in the prescribing information. The Panel did not accept Vifor's submission that the prescribing information provided all the relevant safety information about hypersensitivity reactions. Claims had to be capable of standing alone without reference to, *inter alia*, prescribing information to correct an otherwise misleading impression.

In the Panel's view, the claim highlighted the hypersensitivity issue and sought to minimise the prescriber's concerns about such reactions with Ferinject and in that regard might compromise patient safety. The Panel considered that the claim was misleading and a breach was ruled.

Pharmacosmos alleged that the claim 'Ferinject has a low molecular weight thus limiting adverse events' which appeared as a bullet point immediately beneath the claim at issue above was misleading. There was no proven link between the molecular weight of Ferinject and the adverse event rate.

The Panel noted that Geisser stated that the tolerability of iron compounds depended not only on the reactivity of the iron and how easily it was released from the carbohydrate but also on the size of the iron-carbohydrate complex and the nature of the carbohydrate moiety. A relationship between release rate and acute toxicity was noted. The Panel considered that the claim implied a simple correlation between molecular weight and side effects. In the Panel's view the situation was more complex than that. The Panel considered that the claim sought to minimise a prescriber's concerns about all side effects with Ferinject and in that regard might compromise patient safety. The Panel ruled that the claim was misleading and in breach of the Code.

During its consideration of the case, the Panel noted that both of the claims at issue had been ruled to be misleading with regard to the safety profile of Ferinject; it considered that each would minimise a prescriber's concerns in that regard. Activities prejudicial to patient safety were regarded as serious matters and so the Panel reported Vifor to the Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure.

The Appeal Board was extremely concerned about the material at issue; that it had the potential to compromise patient safety was a serious worry. It had been certified as required by the Code. The Appeal Board was concerned that, as in Case AUTH/2411/6/11, this case raised very serious concerns regarding the expertise of Vifor signatories and the role of senior management in compliance matters.

The Appeal Board noted that Vifor had accepted that it had made serious errors and in that regard it had already started to review its policies and procedures. Nonetheless, the Appeal Board decided that Vifor's procedures in relation to the Code should be audited as soon as possible by the Authority. The audit would take place at the same time as that required in Case AUTH/2411/6/11. On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary.

Vifor was first audited in November 2011 and upon receipt of that audit report the Appeal Board was concerned that Vifor had much work to do. It noted from Vifor's response that a preliminary corrective and preventative actions programme had been drawn up. It requested that Vifor be asked to provide timescales. It also decided that Vifor should be asked to provide copies of the correspondence between the company and its head office about the audit report and details about the role of an external consultant.

The Appeal Board was concerned to note that since deciding that Vifor should be audited, another case, which involved a breach of undertaking (Case AUTH/2442/10/11), had been considered by the Panel. On the day of the audit that case was still on going and so was not discussed. The Appeal Board noted, however, that the case had now completed.

The Appeal Board decided that Vifor should be re-audited in March 2012. On receipt of the report for that audit, the Appeal Board would consider if further sanctions were necessary.

Upon receipt of the March 2012 audit report the Appeal Board was disappointed at the lack of progress since the November 2011 audit particularly with regard to the revision of standard operating procedures (SOPs). The Appeal Board noted that new staff were due to be appointed. The Appeal Board considered that Vifor should be re-audited in six months time at which point it expected there to be significant improvement. In the meantime Vifor should provide by the end of June a detailed interim response to the recommendations of the March 2012 audit to include an update on recruitment and SOPs. If the Appeal Board was not satisfied then the re-audit would be brought forward.

Upon receipt of the next audit report, the Appeal Board would decide whether further sanctions were necessary.

On consideration of the interim response from Vifor the Appeal Board decided there was no need to re-audit sooner than the currently arranged date, in October 2012.

Upon receipt of the October 2012 audit report, the Appeal Board noted that good progress had been made since the last audit. New staff had been appointed who would have key roles in compliance. New standard operating procedures had been written and resources had been committed to Code compliance. The Appeal Board considered that on the basis that Vifor's current commitment to compliance was maintained, no further action was required.

Pharmacosmos A/S complained about the promotion of Ferinject (ferric carboxymaltose) solution for injection/infusion by Vifor Pharma UK Limited. Ferinject was indicated for the treatment of iron deficiency when oral preparations were ineffective or could not be used.

The material at issue was a six-page gatefolded leavepiece (ref 0148/FER/2011) entitled 'Dosage and Administration Summary'. The claims at issue were both referenced to Geisser (2009).

1 Claim 'Ferinject avoids dextran-induced hypersensitive reactions'

This claim appeared as the second bullet point in a section headed 'How quickly can Ferinject be administered?

COMPLAINT

Pharmacosmos noted that there was no mention that Ferinject itself might cause hypersensitivity reactions, although it might be correct as it was stated that Ferinject avoided hypersensitivity reactions caused by another iron product.

Pharmacosmos alleged that this did not represent balanced and fair information and the material was therefore not sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine in breach of Clause 7.2.

The Ferinject summary of product characteristics (SPC), Section 4.8 Undesirable effects, clearly stated that hypersensitivity reactions were observed following administration of Ferinject:

> 'Immune system disorders:
>
> Uncommon (>1/1,000, <1/100): Hypersensitivity including anaphylactoid reactions'.

Furthermore, Section 4.4 clearly identified hypersensitivity reactions as a potential adverse event with Ferinject that might have very severe consequences for the patient:

> 'Parenterally administered iron preparations can cause hypersensitivity reactions including anaphylactoid reactions, which may be potentially fatal (see Section 5.3). Therefore, facilities for cardio-pulmonary resuscitation must be available'.

In addition, Pharmacosmos noted that a recent publication from the Swiss Medicines Agency reported 19 serious anaphylactoid reactions caused by Ferinject over a short period of time in Switzerland.

Pharmacosmos stated that it was clearly documented that Ferinject caused hypersensitivity reactions and this information must be adequately addressed when informing about hypersensitivity reactions in relation to Ferinject. These facts underpinned the importance of physicians knowing about this possible serious adverse event before using Ferinject.

In inter-company dialogue Vifor's statement that the claim was a 'statement of fact' concerned Pharmacosmos because firstly, Vifor had completely missed the point that inferences would be drawn from the claim implying that hypersensitivity reactions were not a feature of Ferinject and secondly, the company's response that its claim was a 'statement of fact' was not correct.

RESPONSE

Vifor submitted that the claim 'Ferinject avoids dextran-based hypersensitive reactions' was a statement of fact as ferric carboxymaltose contained no dextran and thus avoided dextran-based hypersensitivity.

The inclusion of dextran in intravenous (IV) iron preparations was an important physician and patient consideration and health authorities had taken a very clear view on this. In May 2010 The European Medicines Agency (EMA) Pharmacovigilance Working Party (PhVWP) looked at safety concerns associated with iron dextran. In addition, a year ago the French national authority for health (Haute Autorité de Santé) report on Ferinject stated clearly that Ferinject was not a dextran and hence it became the first IV iron accepted for reimbursement in

populations other than haemodialysis patients. Furthermore, in 2010 the French agency for the safety of health products (Agence Française de Sécurité Sanitaire des Produits de Santé) issued a report on iron dextran (CosmoFer marketed in the UK by Pharmacosmos) and requested a Dear Doctor letter be sent to all physicians in France by the company that marketed iron dextran in France. Iron dextran had been added to the list of 77 medicines under assessment by the pharmacovigilance commission of the French agency for safety concerns.

The fact that Ferinject avoided dextran-based hypersensitivity was therefore an important consideration for health professionals and it was important for Vifor to highlight this feature in its communications with health professionals.

The potential for hypersensitivity reactions with Ferinject *per se* was a separate issue and all the relevant Ferinject safety information was clearly and appropriately outlined in the prescribing information on the back page of the leavepiece. Vifor denied a breach of Clause 7.2.

Vifor stated that it was not clear from the complaint what (if any) breach of the Code was alleged in the narrative on the potential for anaphylactic reactions with Ferinject. However, the SPC quoted was accurate and the leavepiece complied with the required Ferinject label and SPC requirements.

The reference to the Swiss Medicines Agency report was, unfortunately, very selective as it omitted to mention that only page 15 of the document referred to the number of anaphylactoid cases with Ferinject and suggested caution regarding interpretation as so little specific could be said regarding this data at that time. Furthermore, the data did not refer to dextran-based hypersensitive reactions at all and so it was not relevant to the complaint.

PANEL RULING

The Panel noted that Section 4.4 of the Ferinject SPC, Special warnings and precautions for use, stated that 'Parenterally administered iron preparations can cause hypersensitivity reactions including anaphylactoid reactions, which may be potentially fatal…...Therefore, facilities for cardio-pulmonary resuscitation must be available'. Section 4.8, Undesirable effects listed hypersensitivity including anaphylactoid reactions as an uncommon side effect. The only reference to this possible side effect to Ferinject in the leavepiece at issue was in the prescribing information. The Panel did not accept Vifor's submission that the prescribing information on the back page of the leavepiece provided all the relevant safety information about hypersensitivity reactions. Claims in promotional material had to be capable of standing alone without reference to, *inter alia*, prescribing information to correct an otherwise misleading impression.

The Panel did not accept Vifor's submission that the potential for hypersensitivity reactions with Ferinject *per se* was a separate issue. The claim highlighted the issue of hypersensitivity reactions and in the Panel's view, without a counter-balancing statement with regard to the possibility of hypersensitivity reactions with Ferinject, sought to minimise the prescriber's concerns about such reactions and in that regard might compromise patient safety.

The Panel considered that the claim was misleading and a breach of Clause 7.2 was ruled.

2 Claim 'Ferinject has a low molecular weight thus limiting adverse events'

The claim appeared as a bullet point immediately beneath the claim at issue in point 1 above.

COMPLAINT

Pharmacosmos stated that there was no proven link between the molecular weight of Ferinject and the adverse event rate; there was no data in the cited reference to support the claim. If anything, some of the unreferenced statements in Geisser seemed to support a lower risk of side effects which related to free iron in iron-carbohydrate molecules with a high molecular weight and Ferinject was characterised in the article as having a high molecular weight. Pharmacosmos alleged that the claim was misleading in breach of Clause 7.2.

RESPONSE

Vifor submitted that Ferinject was similar in structure to ferritin and caused iron to be deposited in the reticuloendothelial system of the liver. It could provide iron without inducing oxidative stress. Its molecular weight of 150,000 Daltons meant that little of the product was lost through renal elimination, unlike other small iron complexes.

Once in the body, iron was released gradually, which avoided the acute toxicity of many other iron compounds and allowed large amounts of iron to be delivered which resulted in a much wider therapeutic window and reduced the likelihood of adverse events.

The cited reference clearly illustrated that the molecular weight of Ferinject was less than iron dextran and for iron complexes Ferinject had a low molecular weight, both of which were facts. Vifor therefore did not consider this was misleading and denied a breach of Clause 7.2.

In response to a request for more information, Vifor confirmed that the audience for the leavepiece was secondary care health professionals as the company's sales force was entirely hospital focused.

Vifor confirmed that the sales force was provided with extensive verbal briefing on a number of items, including the leavepiece at issue, during a sales meeting in March. Slides relevant to the leavepiece were provided.

PANEL RULING

The Panel noted that the reference cited in support of the claim was an editorial by Geisser entitled 'The

pharmacology and safety profile of ferric carboxymaltose (Ferinject): structure/reactivity relationships of iron preparations'. The author stated that the tolerability of iron compounds depended not only on the reactivity of the iron and how easily it was released from the carbohydrate but also on the size of the iron-carbohydrate complex and the nature of the carbohydrate moiety. The release of iron from the polynuclear iron hydroxide-carbohydrate complexes was stated to be inversely related to the molecular weight of the complex. The author also stated that once Ferinject was in the body, iron was gradually released, avoiding the acute toxicity of many other iron compounds. The Panel considered that the claim 'Ferinject has a low molecular weight thus limiting adverse events' implied a simple correlation between molecular weight and side effects. In the Panel's view the situation was more complex than that. The author had noted a relationship between release rate and acute toxicity.

The Panel noted that one slide of the training presentation given to the sales force in March was entitled 'New dosing leavepiece', with the subtitle 'Answers to common questions'. One of these answers was 'Low adverse events'.

The Panel considered that the claim sought to minimise a prescriber's concerns about all side effects with Ferinject and in that regard might compromise patient safety. The Panel considered that the claim was misleading and a breach of Clause 7.2 was ruled.

During its consideration of the case, The Panel noted that both of the claims at issue had been ruled to be misleading with regard to the safety profile of Ferinject. The Panel considered that each would minimise a prescriber's concerns in that regard. The Panel further noted that activities which were prejudicial to patient safety were regarded as serious matters and so it decided to report Vifor to the Code of Practice Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure.

COMMENTS FROM VIFOR ON THE REPORT

Vifor understood the Panel's decision to refer the case to the Appeal Board. However, Vifor considered it important to clarify its activities with regard to the initial inter-company dialogue which preceded the referral of the case to the PMCPA. Due to a number of significant omissions in its communication, Vifor considered that it might have failed to represent its position fully and clearly.

Vifor submitted that it was committed to resolving issues as frequently as possible through inter-company dialogue and to abiding to the letter and spirit of the Code. In this case, the initial letter to Vifor from Pharmacosmos was sent in late May 2011. Vifor reviewed the material at issue in light of Pharmacosmos's comments and responded accordingly. Additionally, no further copies of the leavepiece were printed or distributed to its sales force after this date; new material without the two claims in question was issued on 10 June 2011. Unfortunately, due to an administrative error, Vifor failed to notify Pharmacosmos of these actions and had only recently rectified this matter. Vifor submitted that this omission in communication was an oversight on its part and might have been the reason inter-company dialogue was passed to the PMCPA for review and ruling.

Nonetheless, Vifor accepted the Panel's decision to report the company to the Appeal Board as patient safety was an extremely important matter. Vifor noted that all of its staff were regularly trained (most recently in March and May 2011) on the potential for hypersensitivity with iron products as part of the company's risk management plan. Unfortunately due to the holiday period this information was not provided to the Panel when further information on the claims in question was requested at short notice in August.

Vifor was reviewing its internal processes and materials to ensure the referencing of claims was accurate. It reassured the Appeal Board that it took its commitment towards this process and safety issues very seriously; safety was always its priority in producing new promotional materials.

At the consideration of the report Vifor apologised and accepted that the company had made significant errors. Vifor noted that it had not advised Pharmacosmos that it had discontinued use of the material at issue because its standard operating procedure (SOP) for inter-company dialogue had not included an instruction to notify the complainant about actions undertaken. The SOP had now been amended to deal with this serious oversight. Vifor submitted that as part of its internal review of processes it had increased support for medical sign-off. Vifor noted that it had recently been inspected by the Medicines and Healthcare products Regulatory Agency (MHRA). Vifor was confident that it had robust procedures in place to ensure that previous errors were not repeated.

APPEAL BOARD CONSIDERATION

The Appeal Board was extremely concerned about the material at issue; that it had the potential to compromise patient safety was a serious worry. It had been certified as required by Clause 14.1. The Appeal Board was concerned that, as in Case AUTH/2422/6/11, this case raised very serious concerns regarding the expertise of Vifor signatories and the role of senior management in compliance matters.

The Appeal Board noted that Vifor had accepted that it had made serious errors and in that regard it had already started to review its policies and procedures. Nonetheless, the Appeal Board decided, in accordance with Paragraph 11.3 of the Constitution and Procedure, to require an audit of Vifor's procedures in relation to the Code to be carried out by the Authority. The audit should be conducted as soon as possible. The audit would take place at the same time as that required in Case AUTH/2411/6/11. On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary.

FURTHER CONSIDERATION BY THE APPEAL BOARD

Vifor was first audited in November 2011 and upon receipt of that audit report the Appeal Board was concerned that the report indicated that Vifor had much work to do. It noted from Vifor's response that a preliminary corrective and preventative actions programme had been drawn up. It requested that Vifor be asked to provide timescales for the actions. It also decided that Vifor should be asked to provide copies of the correspondence between the company and its head office about the audit report and details about the role of an external consultant.

The Appeal Board was concerned to note that since deciding that Vifor should be audited, another case, which involved a breach of undertaking (Case AUTH/2442/10/11), had been considered by the Panel. On the day of the audit that case was still ongoing and so was not discussed. The Appeal Board noted, however, that the case had now completed.

The Appeal Board decided that Vifor should be re-audited in March 2012. On receipt of the report for that audit, the Appeal Board would consider if further sanctions were necessary.

Upon receipt of the March 2012 audit report the Appeal Board was disappointed at the lack of progress since the November 2011 audit particularly with regard to the revision of standard operating procedures (SOPs). The Appeal Board noted that new staff were due to be appointed. The Appeal Board considered that Vifor should be re-audited in six months time at which point it expected there to be significant improvement. In the meantime Vifor should provide a detailed interim response to the recommendations of the March 2012 audit to include an update on recruitment and SOPs. This interim response should be provided by the end of June 2012 and Vifor advised that if the Appeal Board was not satisfied then the re-audit would be brought forward.

Upon receipt of the next audit report, the Appeal Board would decide whether further sanctions were necessary.

On consideration of the interim response from Vifor the Appeal Board decided that there was no need to re-audit sooner than the currently arranged date, in October 2012.

Upon receipt of the October 2012 audit report, the Appeal Board noted that good progress had been made since the last audit. New staff had been appointed who would have key roles in compliance. New standard operating procedures had been written and resources had been committed to Code compliance. The Appeal Board considered that on the basis that Vifor's current commitment to compliance was maintained, no further action was required.

Complaint received	**27 July 2011**
Undertaking received	**31 August 2011**
Appeal Board consideration	**12 October 2011** **7 December 2011** **19 April 2012** **26 July 2012** **15 November 2012**
Interim case report first published	**23 January 2012**
Case completed	**15 November 2012**

CASE AUTH/2435/8/11

GLAXOSMITHKLINE/DIRECTOR v CHIESI

Promotion of an unlicensed indication and breach of undertaking

GlaxoSmithKline complained that, ahead of receiving a marketing authorization, Chiesi had promoted Fostair (beclometasone and formoterol) for use in chronic obstructive pulmonary disease (COPD). Fostair was currently only licensed in the UK for the regular treatment of asthma. The complaint also included an alleged breach of undertaking and that aspect was taken up by the Director as it was the Authority's responsibility to ensure compliance with undertakings.

The detailed response from Chiesi is given below.

GlaxoSmithKline stated that at a Chiesi symposium at the American Thoracic Society (ATS) in May 2011, claims were made regarding the efficacy of Fostair and the extra-fine nature of the product in COPD. As only non-US delegates could attend the Chiesi symposium, there were many European and, particularly, UK attendees. Delegates were notified of the Chiesi symposium by a flyer invitation and through information contained in the abstract book provided in the conference bags. These materials did not indicate that it was a promotional meeting. GlaxoSmithKline alleged a failure to comply with all applicable codes, laws and regulations. This was particularly relevant as Chiesi activities and materials involved more than one country and failed to comply with the European Federation of Pharmaceutical Industries and Associations (EFPIA) Code, the code of the host country and the 2011 ABPI Code.

During the symposium a UK health professional presented the results from a phase III study on the use of Fostair in COPD which demonstrated equivalence with AstraZeneca's product Symbicort (budesonide and formoterol), an established therapy licensed for the treatment of severe COPD. The summary slides concluded that an extra-fine fixed combination of formoterol and beclometasone 'translates to clinical benefits in asthma and COPD'. It was never stated that Fostair was licensed only for the treatment of asthma. There was little doubt that UK attendees unfamiliar with the Fostair marketing authorization would wrongly assume that it was licensed for COPD.

GlaxoSmithKline alleged that such high profile, non-compliant activity at an international symposium attended by a significant number of UK health professionals failed to maintain high standards; such off-licence promotion inevitably brought discredit upon and reduced confidence in the pharmaceutical industry.

GlaxoSmithKline referred to Case AUTH/2379/1/11 in which Chiesi was ruled in breach for distributing the journal Respiratory Disease in Practice, which was deemed to promote Fostair for COPD, from a British conference stand. As the ruling of that case was over a month before the ATS symposium, GlaxoSmithKline was even more concerned that the Chiesi promotional symposium at the ATS conference was certified to include claims about the efficacy of Fostair in COPD. This called into question the gravity ascribed by Chiesi to the previous ruling. GlaxoSmithKline was concerned that the symposium, with its heavy emphasis on the use of Fostair in COPD, condoned the repeated presentation of data about an unlicensed indication in a promotional setting. GlaxoSmithKline alleged that the ongoing promotion of Fostair in COPD was in breach of the undertaking given in Case AUTH/2379/1/11.

The Panel noted that Chiesi referred to a previous case, Case AUTH/2406/5/11, which concerned the same symposium and wherein the Panel had ruled no breach as it considered the matter of complaint was not within the scope of the Code. In accordance with the Constitution and Procedure, there was no published case report.

Turning to the present case, Case AUTH/2435/8/11, the Panel noted that each case had to be decided on its individual set of facts. There were important differences in the evidence before the Panel in the present case and that considered previously. Chiesi had previously submitted, *inter alia*, that Chiesi Ltd had not been involved in any aspect of the arrangements. In the present case, the Panel noted Chiesi's initial submission that any UK health professionals who had attended the symposium had done so at their own wish and not through any Chiesi activity. Chiesi subsequently submitted that Chiesi Ltd's employees had attended the conference, had told UK health professionals at the conference about the symposium and had provided a copy of the flyer to those health professionals. Indeed they had been instructed to do so by Chiesi corporate. The Panel considered that as Chiesi Ltd had invited UK health professionals to the symposium, the symposium was consequently within the scope of the Code. Chiesi Ltd was therefore responsible under the Code for the content of the presentations given at the symposium.

The Panel noted that one presentation covered, *inter alia*, 'BDP/F extrafine inhaler in COPD'. The last five slides dealt with the effects of Fostair on a number of parameters of COPD. The two cited references in this part of the presentation had been published in 2010, ie it was not new data. The fifth slide, the final one of the presentation, was headed 'BDP/F Extrafine: Summary' and stated that Fostair provided a more efficient delivery throughout the entire bronchial tree vs other combination products and that it 'Reaches small airways' and 'Treats small airways'. The final bullet point stated that this 'Translates to clinical benefits in asthma and COPD'.

The Panel noted Chiesi's submission with regard to the legitimate exchange of medical and scientific information during the development of a medicine, which was permitted under the supplementary information to the Code. The Panel queried how presenting data about the use of Fostair in COPD could be considered exchange of information 'during the development of a medicine'. Fostair already had a marketing authorization and was licensed for use in COPD in Turkey. Chiesi had noted that the conference was a truly international event and that Turkey was a major industrialised country; the Panel noted that these factors featured in the supplementary information to the Code, Promotion at International Meetings, not the supplementary information relating to the legitimate exchange of medical and scientific information during the development of a medicine. In the Panel's view, disseminating data to prescribers which expanded a licensed product's market share was different to the legitimate exchange of medical and scientific information during the development of a medicine which implied debate which enhanced the current state of scientific knowledge.

The Panel considered that the presentation promoted the use of Fostair in COPD and was thus not in accordance with the terms of its marketing authorization. A breach was ruled. Chiesi had invited UK health professionals to a symposium at which information on the use of Fostair in an unlicensed indication was presented. The Panel considered that high standards had not been maintained and ruled a breach. The Panel considered that, on balance, given the circumstances of this case, this matter 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. No breach of that clause was ruled.

In relation to the alleged breach of the undertaking given in Case AUTH/2379/1/11, the Panel noted that the previous case concerned the distribution of copies of Respiratory Disease in Practice from a Chiesi stand at a British congress. The journal was sponsored by Chiesi and contained an advertisement for Fostair. The article on the front cover was entitled 'The small airways: an important target in asthma and COPD treatment'. The Panel considered that the distribution of the journal from Chiesi's promotional stand in effect promoted Fostair for an unlicensed indication. In addition, the Panel noted that a Fostair advertisement in the journal referred to the extrafine particles reaching the small airways. In the Panel's view this linked to the article about the treatment of COPD and references to particle size, and it ruled, *inter alia*, a breach of the Code.

The Panel considered that an undertaking was an important document. It included an assurance that all possible steps would be taken to avoid similar breaches of the Code in future. It was very important for the reputation of the industry that companies complied with undertakings.

The undertaking given in Case AUTH/2379/1/11 in March 2011 required that use of the journal in question and any similar material, if not already discontinued or no longer in use, would cease forthwith. The Panel considered that the subsequent symposium which promoted Fostair in COPD meant that this undertaking had not been complied with and it ruled a breach of the Code.

The Panel noted its rulings of breaches of the Code above and considered that Chiesi had failed to meet the requirement to comply with all applicable codes and thus ruled a further breach.

GlaxoSmithKline noted that a further edition of Respiratory Disease in Practice (Spring), sponsored by Chiesi, clearly implied that a COPD marketing authorization was already in place for Fostair. GlaxoSmithKline considered this was further evidence of extensive, on-going, off-licence promotion which was unacceptable.

The Panel noted that companies could sponsor material. It had previously been decided, in relation to material aimed at health professionals, that the content would be subject to the Code if it was promotional in nature or if the company used the material for a promotional purpose. Even if neither of these applied, the company would be liable if it had been able to influence the content of the material in a manner favourable to its own interests. It was possible for a company to sponsor material which mentioned its own products and not be liable under the Code for its content, but only if it had been a strictly arm's length arrangement with no input by the company and no use by the company of the material for promotional purposes. Factors which might mean there had not been a strictly arm's length arrangement would include, *inter alia*, selection of the author by the pharmaceutical company.

The Panel noted that Chiesi had suggested the author for the article that appeared on the front page of the journal at issue. Chiesi thus could not take the benefit of an arm's length agreement, and was responsible under the Code. The article provided details of Fostair clinical trials in COPD, which was not within the terms of the Fostair marketing authorization. An image was also included with the caption 'Beclometasone dipropionate (BDP) crystals. BDP in combination with formoterol is available as Fostair, one of several combination inhalers on the market'.

The Panel considered that the Spring edition of Respiratory Disease in Practice was not in accordance with Fostair's marketing authorization. The undertaking given in Case AUTH/2379/1/11 was that use of the journal in question and any similar material, if not already discontinued or no longer in use, would cease forthwith. The Panel considered that this undertaking had not been complied with and ruled a breach of the Code. High standards had not been maintained and Chiesi had brought discredit upon and reduced confidence in the pharmaceutical industry. Breaches of the Code were ruled including a breach of Clause 2

GlaxoSmithKline was deeply concerned over Chiesi's apparent lack of understanding as to the scope of

the Code and the company's apparent unwillingness to abide by the spirit of it. These concerns were particularly heightened as Chiesi had recently been ruled in breach of the Code in Cases AUTH/2379/1/11 and AUTH/2352/8/10. GlaxoSmithKline alleged that all these activities taken together did not maintain the high standards expected from a pharmaceutical company and brought the industry into disrepute.

The Panel noted that GlaxoSmithKline referred to two previous cases where Chiesi had been ruled in breach of the Code. Case AUTH/2379/1/11 was described above and resulted in a ruling of breaches of the Code. Case AUTH/2352/8/10 concerned a clinical support service which was ruled to be a switch service, in breach of the Code. Breaches of the Code, including of Clause 2, were ruled.

The Panel noted that the allegation of a breach of, *inter alia*, Clause 2 was in relation to a pattern of behaviour as evidenced by Chiesi's conduct in this case, Case AUTH/2435/8/11 and both previous cases. Although all three cases were relatively recent and in the same therapy area, Case AUTH/2352/8/10 related to the provision of a medical and educational service that was linked to a particular product, not the promotion of a product outside of its marketing authorization. Case AUTH/2379/1/11 and the present case, however, both related to the promotion of Fostair outside of its marketing authorization. The Panel considered that repeated breaches of the Code in the same therapy area was a serious matter. Nonetheless, the Panel considered that the discrete rulings of breaches of Clause 2, which was reserved to indicate particular censure, in Case AUTH/2352/8/10 and the present case, Case AUTH/2435/8/11 adequately covered this allegation. The Panel did not consider that the cumulative effect of these cases was such as to warrant additional censure. No further breach of the Code was ruled.

The Panel was very concerned that it had to ask Chiesi three times for information before it got all of the facts needed to make its rulings. Responses were contradictory in relation to the invitation of UK health professionals to the symposium at issue. UK staff had been briefed to encourage UK health professionals to attend which contradicted the company's initial response that UK health professionals attended the symposium at their own wish and not through any Chiesi activity. With regard to the article in Respiratory Disease in Practice it was only when the Panel had asked twice for further information regarding its involvement that the company stated that it had suggested the author. This was unacceptable; self regulation relied upon a full and frank disclosure of the facts at the outset. The Panel considered that Chiesi's conduct in relation to this case warranted consideration by the Appeal Board and it decided to report the company to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to consider whether further sanctions were warranted.

The Appeal Board noted that Chiesi accepted that it had made errors and that it had taken action to improve its processes to avoid similar errors. Nonetheless, the Appeal Board was very concerned at the number of requests the Panel had had to make to obtain all of the relevant information and the fact that the incomplete and thus misleading initial response was signed and therefore agreed by the managing director. There had been three further requests from the Panel.

The Appeal Board considered that it was vital that responses to the Authority were comprehensive and not misleading by omission. The failure to provide complete and accurate information was unacceptable. The Authority and the complaints procedure, relied upon companies providing a comprehensive account of the matter in question and offering all of the relevant information even if it had not specifically been requested. The Appeal Board decided that Chiesi should be publicly reprimanded for its failure to provide comprehensive information at the outset and that, in accordance with Paragraph 11.3 of the Constitution and Procedure, its procedures in relation to the Code should be audited by the Authority. The audit should be conducted in March 2012. On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary.

On receipt of the March 2012 audit report the Appeal Board considered that Chiesi's procedures were not satisfactory. The Appeal Board noted that since the audit new staff were to be appointed. The Appeal Board decided that Chiesi should be re-audited in six months time. Upon receipt of the report for that audit, it would decide whether further sanctions were necessary.

Upon receipt of the October 2012 audit report, the Appeal Board noted that there had been progress since the last audit. The Appeal Board noted that in its comments upon the audit report Chiesi had stated that in addressing the PMCPA's comments about its standard operating procedures (SOPs) it could give the PMCPA a new set of SOPs within four weeks. The Appeal Board thus decided that the PMCPA should examine the revised SOPs and report its findings at the Appeal Board meeting in January 2013. The Appeal Board noted that, providing the revised SOPs were satisfactory, it would be minded to require no further sanctions.

At its meeting in January 2013 the Appeal Board noted from the PMCPA's review of Chiesi's updated SOPs that although there were still some issues to address, sufficient progress had been made and on the basis that this was maintained, no further action was required.

GlaxoSmithKline complained that, ahead of receiving a marketing authorization, Chiesi had promoted Fostair (beclometasone and formoterol) for use in chronic obstructive pulmonary disease (COPD). Fostair was currently licensed in the UK for the regular treatment of asthma where use of a combination product (inhaled corticosteroid and long-acting beta2 agonist) was appropriate. The complaint also included an alleged breach of undertaking and that aspect was taken up by the Director as it was the Authority's responsibility to ensure compliance with undertakings.

1 Alleged promotion of Fostair for chronic obstructive pulmonary disease (COPD) at a Chiesi-sponsored symposium, American Thoracic Society Conference, May 2011

COMPLAINT

GlaxoSmithKline stated that at the Chiesi symposium entitled 'Targeting Small airways: towards an optimized therapeutic management of respiratory disease', explicit claims were made about the efficacy of Fostair and the extra-fine nature of the product in COPD. Fostair was licensed only for the treatment of asthma. As only non-US delegates could attend the Chiesi symposium, there were many European and, particularly, UK attendees. Delegates were notified of the symposium by a flyer invitation and information contained in the abstract book provided in the conference bags. These materials did not indicate that the meeting was promotional. GlaxoSmithKline alleged, therefore, that Chiesi failed to comply with all applicable codes, laws and regulations to which it was subject. This was particularly relevant as Chiesi activities and materials used at the conference involved more than one country and failed to comply with the European Federation of Pharmaceutical Industries and Associations (EFPIA) Code, the code of the host country and the 2011 ABPI Code. GlaxoSmithKline alleged a breach of Clause 1.8.

During the symposium a UK health professional presented the results from a phase III study on the use of Fostair in COPD. The results were regarded as equivalent to AstraZeneca's product Symbicort (budesonide and formoterol), an established therapy licensed for the treatment of patients with severe COPD (FEV1<50% predicted normal) and a history of repeated exacerbations who had significant symptoms despite therapy with long-acting bronchodilators.

The summary slides for the presentation concluded that an extra-fine fixed combination of formoterol and beclometasone 'translates to clinical benefits in asthma and COPD'. It was never stated in the symposium, explicitly or otherwise, that Fostair was licensed only for the treatment of asthma. There was little doubt that UK attendees unfamiliar with the marketing authorization for Fostair would have left the symposium with the erroneous impression that Fostair was licensed for the management of COPD. A breach of Clause 3.2 was alleged.

GlaxoSmithKline stated that given the high profile nature of such non-compliant activity at an international symposium attended by a significant number of UK health professionals, such actions failed to maintain acceptably high standards. As a consequence, GlaxoSmithKline considered that such off-licence promotion inevitably brought discredit upon and reduced confidence in the pharmaceutical industry in breach of Clauses 9.1 and 2.

GlaxoSmithKline referred to Case AUTH/2379/1/11 in which Chiesi was ruled in breach of Clauses 3.2, 7.2 and 7.10 for distributing the journal Respiratory Disease in Practice, which was deemed to promote Fostair for COPD, from its stand at the British Thoracic Society (BTS) Congress. As the ruling of that case was over a month before the ATS symposium, GlaxoSmithKline was even more concerned that the content of a Chiesi promotional symposium at the ATS conference was certified to include claims about the efficacy of Fostair in COPD. GlaxoSmithKline considered that this called into question the gravity ascribed by Chiesi to this ruling and was concerned that the content of the symposium, with its heavy emphasis on the use of Fostair in COPD, condoned the repeated presentation of data about an unlicensed indication in a promotional setting.

As such, GlaxoSmithKline considered that the ongoing promotion of Fostair in COPD was in breach of the undertaking given in Case AUTH/2379/1/11 and in breach of Clause 25 of the Code.

RESPONSE

Chiesi was disappointed that GlaxoSmithKline had raised this matter with the Authority considering that this issue was the subject of Case AUTH/2406/5/11 under which the Panel ruled the matter not within the scope of the Code and hence not a breach by the UK affiliate of Chiesi (hereafter known as Chiesi Ltd).

Chiesi Ltd submitted that the symposium in question was organised and sponsored by its Italian corporate headquarters (hereafter referred to as Chiesi corporate). All arrangements for the symposium were made between Chiesi corporate and the ATS Conference. The speakers, agenda and presentations were organised by Chiesi corporate. Chiesi Ltd was not involved in any aspect of the organisation of the symposium nor did it sponsor the event in any form.

In light of the recent changes to Clause 20, The Use of Consultants, and to prepare for the reporting required from 2012, Chiesi had a system whereby payments to UK health professionals by other Chiesi affiliates, including Chiesi corporate, were reported to Chiesi Ltd. Through this process Chiesi was informed that Chiesi corporate had invited a UK health professional to deliver a lecture at the ATS Conference entitled 'Reaching and treating small airways: the latest evidence with an extrafine fixed combination'. Chiesi was also told about the honorarium that would be paid by Chiesi corporate. Chiesi was not involved in the preparation of the contract with the health professional in question, nor did it pay his honorarium; this was all handled by Chiesi corporate. The UK speaker was one of the two speakers at the event; the other was from the Netherlands.

GlaxoSmithKline mentioned that the symposium was attended by a significant number of UK health professionals. The ATS Conference was a truly international event with over 14,000 delegates from more than 90 countries. The symposium was open to any non-US delegate attending the conference. Chiesi did not arrange for any UK health professionals to attend the conference or the symposium; the UK health professionals attended the symposium at their own wish and not through any Chiesi activity. Flyers for the symposium were placed in the conference delegate bags, along with flyers for all the symposia. The flyers were organised

by Chiesi corporate and again, Chiesi played no role in the organising, printing or distribution of these flyers in the delegate bags.

In response to a request for further information, Chiesi submitted that it did not directly, or via a third party, sponsor or invite any UK health professionals to attend the ATS Conference. In addition Chiesi corporate did not directly, or via a third party, invite any UK health professionals to the conference or the symposium. No third party provider was involved in any way with the conference symposium as the symposium was conducted using the audio-visual services provided by the ATS.

As Chiesi did not have a promotional presence in respiratory [sic] in the US, there was no product booth at the ATS Conference. In accordance with all company-sponsored symposia at the conference, Chiesi had two pull-up banners listing the symposium day, time and agenda. A one page advertisement promoting the symposium was included in the conference programme and flyers for the symposium were also made generally available at the conference, as with the flyers for all other company-sponsored symposia. A copy of the flyer was provided.

Chiesi Ltd submitted that only four of its employees attended the conference. As the Chiesi Ltd team was small, there was no formal briefing document sent to them by Chiesi Ltd, but simply a logistics itinerary provided by a third party company. A copy of an email from that company to one of Chiesi Ltd's employees attending the conference was provided. A general briefing email, sent to the medical directors and commercial directors of all Chiesi affiliates by the global medical marketing team at Chiesi corporate, included a summary of the data to be presented at the ATS Conference including the symposium and a request to invite customers, if possible. Once at the conference, if the Chiesi Ltd staff interacted with a UK health professional, they suggested that (s)he might wish to consider attending the company symposium. There were many other parallel company symposia that the health professional could also have considered attending.

Chiesi submitted that as background to this verbal dialogue, it was important to note that Chiesi had three products licensed for use in respiratory diseases; Atimos Modulite (formoterol) inhaler for asthma and COPD, Clenil Modulite (beclomethasone) inhaler for asthma and Fostair Modulite inhaler for asthma. Fostair was, however, also licensed for COPD in Turkey, a major industrialised country. It was also important to note that the information received by the affiliate staff from the corporate medical marketing team and all subsequent information about the symposium referred to the title of the symposium; 'Targeting Small airways: towards an optimized therapeutic management of airways disease'. The two talks were listed as 'Recognising the role of small airways: a clinical need' and 'Reaching and treating small airways: the latest evidence with an extrafine combination'. No information was provided to the affiliate staff that the second presentation, given by the UK health professional, would include data on Fostair in COPD. Chiesi also noted that of the two presentations, only 4 slides referred to beclomethasone/formoterol and COPD.

Under the Code, Chiesi Ltd and Chiesi corporate understood that the relevant codes relating to this issue were those pertaining to the country of origin of the EU headquarters (Italy) and the country in which the activity took place (US). As the event took place in an international product theatre to which US health professionals were prohibited, this left the code of relevance as being the Italian Farmindustria Code, the ABPI Code was not applicable to this case, as noted in the Panel's ruling in Case AUTH/2406/5/11.

In summary, Chiesi Ltd wholly believed that it did not promote off licence data in COPD. Chiesi Ltd played no role in the organisation of the symposium or the content of the presentations. Chiesi corporate also believed that the activities conducted at the ATS Conference complied with the relevant code of practice, the Italian Farmaindustria Code.

Following a request for further information, Chiesi provided a copy of the briefing email noted above, which was sent to the medical directors and commercial directors of all Chiesi affiliates by the global medical marketing team at Chiesi corporate. The email stated there was a Chiesi symposium at the international product theatre and requested that affiliate staff inform health professionals they knew would be attending the conference about the Chiesi symposium. The flyer for the symposium was attached to the email. There was no mention in the email or the flyer that COPD data would be included in the symposium content.

Chiesi confirmed that Chiesi Ltd staff that attended the conference told UK health professionals that they knew and met at the conference that Chiesi corporate was holding a symposium at the international product theatre and they provided a copy of the flyer to those health professionals that expressed an interest in attending.

Chiesi reiterated that it:

- had no involvement in the development or conduct of the symposium
- had no knowledge of the content of the symposium – all materials it received, the copy of the flyer for the symposium and the briefing materials referred to the symposium subject being 'Targeting Small airways: towards an optimized therapeutic management of respiratory disease'
- did tell UK health professionals that there would be a symposium at the international product theatre. There were a number of company sponsored symposia available to the health professionals to attend if they wished. That a UK health professional attended the Chiesi symposium or any other company sponsored symposium was entirely their own decision and Chiesi Ltd did not consider that it had influenced the health professional in that regard nor did it have a greater influence than any other company

that was also meeting with health professionals and handing out their own symposia flyers.

In relation to this case, Chiesi Ltd sought clarification from the PMCPA on Clause 3 under which the legitimate exchange of medical and scientific information during the development of a medicine was not prohibited provided that any such information or activity did not constitute promotion which was prohibited under that or any other clause.

Chiesi submitted that there seemed to be a wide spectrum of practice that took place across the industry and the recent European Respiratory Society (ERS) meeting in Amsterdam in September was a good example of this. The 'accepted practice' appeared to be that the activities associated with the promotional stands were deemed to be promotional. However, the symposia which were sponsored by the respective pharmaceutical companies were considered to be medical and scientific. As such at the ERS meeting a number of pharmaceutical companies sponsored symposia which focussed entirely on their products which were under development and would not be granted a licence until 2012, according to the presentations. Much of the data presented was only abstract data, presented for the first time at the meeting and hence not published nor had it passed through a scientific peer review process. Chiesi submitted that the presentation of this data by the respective companies was considered the legitimate exchange of scientific and medical information. The flyers for the symposia and all data included in the symposia was out of licence.

Chiesi stated that at the Chiesi corporate symposia at the ATS Conference, the presentation produced by the UK heath professional referred to peer reviewed, published, scientific data in COPD. Furthermore, this was only six slides of the whole medical scientific symposium (a copy of the slides was provided). Chiesi Ltd considered therefore that although it had no involvement in the symposium nor any communication prior to the event that COPD data would be included, the symposium itself was fair, balanced and representative of the peer reviewed and scientific data on the subject of small airways in respiratory disease.

PANEL RULING

The Panel noted that Chiesi referred to a previous case, Case AUTH/2406/5/11, which concerned the same symposium and wherein the Panel had ruled no breach of the Code as it considered the matter of complaint was not within the scope of the Code. The complainant had not appealed the Panel's ruling and so, in accordance with the Constitution and Procedure, there was no published case report.

Turning to the present case, Case AUTH/2435/8/11, the Panel noted that each case had to be decided on its individual set of facts. There were important differences in the evidence before the Panel in the present case and that considered previously. Chiesi had previously submitted, *inter alia*, that Chiesi Ltd had not been involved in any aspect of the arrangements.

In the present case, the Panel noted Chiesi's initial submission that any UK health professionals who had attended the symposium had done so at their own wish and not through any Chiesi activity. Chiesi subsequently submitted that Chiesi Ltd's employees had attended the conference, had told UK health professionals at the conference about the symposium and had provided a copy of the flyer to those health professionals. Indeed they had been instructed to do so in an email by Chiesi corporate. The Panel considered that as Chiesi Ltd had invited UK health professionals to the symposium, the symposium was consequently within the scope of the Code and had to comply with it. Chiesi Ltd was therefore responsible under the Code for the content of the presentations given at the symposium.

The Panel noted that in a slide detailing the outline of the presentation given by the UK heath professional, four topics would be covered, including 'BDP/F extrafine inhaler in COPD'. The last five slides dealt with the effects of Fostair on a number of parameters of COPD. The two cited references in this part of the presentation had been published in 2010, ie it was not new data. The fifth slide, the final one of the presentation, was headed 'BDP/F Extrafine: Summary' and stated that Fostair provided a more efficient delivery throughout the entire bronchial tree vs other combination products and that it '***Reaches*** small airways' and '***Treats*** small airways'. The final bullet point stated that this 'Translates to ***clinical benefits*** in asthma and COPD'.

The Panel noted Chiesi's submission with regard to the legitimate exchange of medical and scientific information during the development of a medicine, which was permitted under the supplementary information to Clause 3. The Panel queried how presenting data about the use of Fostair in COPD could be considered exchange of information 'during the development of a medicine'. Fostair already had a marketing authorization and was licensed for use in COPD in Turkey. Chiesi had noted that the conference was a truly international event and that Turkey was a major industrialised country; the Panel noted that these factors featured in the supplementary information to Clause 3, Promotion at International Meetings, not the supplementary information relating to the legitimate exchange of medical and scientific information during the development of a medicine. In the opinion of the Panel, disseminating data to prescribers which expanded a licensed product's market share was different to the legitimate exchange of medical and scientific information during the development of a medicine which implied debate which enhanced the current state of scientific knowledge.

The Panel considered that the presentation at issue promoted the use of Fostair in COPD and was thus not in accordance with the terms of its marketing authorization. A breach of Clause 3.2 was ruled. Chiesi had invited UK health professionals to a symposium at which information was presented on the use of Fostair in an unlicensed indication. The Panel considered that high standards had not been maintained and ruled a breach of Clause 9.1. The Panel considered that, on balance, given the circumstances of this case, this matter 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. No breach of that clause was ruled.

In relation to the alleged breach of the undertaking given in Case AUTH/2379/1/11, the Panel noted that the previous case concerned the distribution of copies of Respiratory Disease in Practice, Volume 21 Number 1 from a Chiesi stand at a British Thoracic Society (BTS) congress. The journal was sponsored by Chiesi and contained an advertisement for Fostair. The article on the front cover was entitled 'The small airways: an important target in asthma and COPD treatment'. The Panel considered that the distribution of the journal from Chiesi's promotional stand in effect promoted Fostair for an unlicensed indication. In addition, the Panel noted that a Fostair advertisement in the journal referred to the extrafine particles reaching the small airways. In the Panel's view this linked to the article about the treatment of COPD and references to particle size, and it ruled, *inter alia*, a breach of Clause 3.2.

The Panel considered that an undertaking was an important document. It included an assurance that all possible steps would be taken to avoid similar breaches of the Code in future. It was very important for the reputation of the industry that companies complied with undertakings.

The undertaking given in Case AUTH/2379/1/11 and dated 25 March 2011 required that use of the journal in question and any similar material, if not already discontinued or no longer in use, would cease forthwith. The Panel considered that the subsequent symposium which promoted Fostair in COPD meant that this undertaking had not been complied with and it ruled a breach of Clause 25.

In relation to the GlaxoSmithKline's allegation of a breach of Clause 1.8, the Panel noted that this clause required that pharmaceutical companies must ensure that they complied with all applicable codes, laws and regulations to which they were subject. The Panel noted its rulings of breaches of the Code above. The Panel considered that by failing to comply with the UK Code, Chiesi had failed to meet this requirement. A breach of Clause 1.8 was ruled.

2 Spring 2011 Respiratory Disease in Practice

COMPLAINT

GlaxoSmithKline was increasingly concerned that Chiesi was promoting Fostair, deliberately or otherwise, for COPD ahead of it receiving a marketing authorization for this indication. Such activities gave the impression of a UK and, indeed, multinational, co-ordinated, concerted pre-licence, multi-channel campaign. GlaxoSmithKline had noted yet a further edition of the publication sponsored by Chiesi cited in Case AUTH/2379/1/11 (a copy of which was provided). This publication clearly implied that a marketing authorization was already in place for Fostair in COPD. GlaxoSmithKline considered this was further evidence of ongoing breaches of the Code in relation to extensive off-licence promotion and considered that such ongoing activity was totally unacceptable.

When writing to Chiesi the Authority asked it to respond in relation to Clauses 2 and 9.1 with regard to the alleged breach of undertaking.

RESPONSE

Chiesi submitted that it had had no communication with GlaxoSmithKline about Chiesi's support of the Spring 2011 edition of Respiratory Disease in Practice and it was unclear as to exactly how its support of this journal constituted a breach of undertaking. Respiratory Disease in Practice was an independent journal title. In response to an approach from the publisher, Chiesi had agreed to provide an unrestricted educational grant to fund a fixed number of issues over a set period of time. Its support was clearly declared on the front page of the journal. On page 3 of the journal, the publisher stated: 'The sponsor has no editorial input into, or control over, the content of this publication. Sponsorship is for four issues to be published in 2011. The data, opinions and statements appearing in the articles herein are those of the contributor(s) concerned; they are not necessarily endorsed by the sponsor, publisher, Editor or Editorial Board'.

In line with this agreement Chiesi had had no input into any edition of the journal, including the Spring 2011 edition. Following the ruling in Case AUTH/2379/1/11, the company had also had no involvement with the distribution of the journal and had not purchased reprints or used the journal in promotion. The distribution of the journal to health professionals was conducted by the publishers with no input from Chiesi. Chiesi had not reviewed or commented on the content of the journal. The only Chiesi advertisement in the Spring 2011 edition of the journal was a corporate advertisement.

Since it had no input into the content of the journal and had not used it for promotional purposes Chiesi considered that it had adhered to its undertaking in relation to Case AUTH/2379/1/11 and denied any breach of the Code.

Chiesi noted that the Spring 2011 edition featured a review of combination inhaler trials in COPD which examined published studies of all the available combination inhalers including Fostair ('BDP/F'). GlaxoSmithKline stated that the publication 'clearly implied that a marketing authorization was already in place for Fostair in COPD' but in fact the article stated clearly 'BDP/F does not yet have a licence for COPD …'.

In response to a request for further information, Chiesi submitted that it did not have on file a signed written contract with the publishers regarding Respiratory Disease in Practice but it provided a copy of the contract that Chiesi did receive. The terms and conditions on which the sponsorship was made were also provided. Chiesi Ltd considered that the acceptance of the terms and conditions constituted a legally binding contract.

Chiesi submitted that the title, scope and content of the article at issue in the Spring 2011 edition of the journal was commissioned by an editorial director, written by a health professional (the author) and prepared for publication by a sub-editor who was responsible for

commissioning content at the request of the editorial board, liaising with authors and the editor over copy and proofs and also sub-editing and producing the journal. The article was reviewed and accepted for publication by the journal's editor. Chiesi received a copy of the article, in accordance with the contract and reviewed it for scientific accuracy only. There was no other involvement by Chiesi in the article.

A copy of a letter from the publishers and the editor was provided which outlined the processes of the journal to ensure Code compliance. The publishers had also included documents relevant to the case including emails detailing the editor's comments and a communication regarding the article with Chiesi Ltd.

With respect to the undertakings by Chiesi Ltd following Case AUTH/2379/1/11, a breach was ruled relating to the distribution of the journal from a promotional stand at the BTS. Following this ruling, Chiesi had not distributed any copies of that edition (volume 21) or the current Spring edition (volume 22) directly to health professionals and had not used the journal in any promotional activities. The second ruling of the case was in relation to the use of the Fostair advertisement on the back page of the journal. In volume 22, this was replaced with a corporate advertisement with no reference to any Chiesi products. Chiesi considered therefore that it had taken reasonable steps to address the issues raised in Case AUTH/2379/1/11.

In response to a further request for further information, Chiesi submitted that the limit of its involvement with the Spring edition was to suggest the author for the cover article entitled 'A review of combination inhaler trials in COPD'. The article referred, *inter alia*, to Fostair clinical trial results in COPD. A second letter from the publishers was submitted that stated that the title, scope and content of the article was agreed between the editor and the author following his agreement to contribute to the journal. Chiesi did not provide any information for inclusion in the article or have any involvement in its publication. The letter also stated that none of the publication's sponsors had any influence, or contribution to, the circulation of the journal and no details of the circulation list were provided to them. The target audience of the journal was health professionals that were relevant to the title.

Chiesi submitted that it received 200 copies of the journal as part of the standard terms of the sponsorship. This was the first time that Chiesi had seen the final and complete publication. Its internal process was then to review the publication. If any of the articles in the publication referred to any Chiesi products, the content was checked to ensure it complied with the product licences. If the publication complied with its product licences, it was then reviewed through its approval process for promotional material to formally approve the content and to approve the intended use. If the articles were not within the terms of its product licences then the publication was not reviewed through the approval process and was simply retained by the medical department in case it might be useful to respond to specific medical information enquiries, should this be appropriate. The 200 copies of the volume 22 publication were reviewed as above but as the article on COPD was not considered suitable for promotional use they remained in the medical department at Chiesi.

PANEL RULING

The Panel noted that it was acceptable for companies to sponsor material. It had previously been decided in relation to material aimed at health professionals that the content would be subject to the Code if it was promotional in nature or if the company used the material for a promotional purpose. Even if neither of these applied, the company would be liable if it had been able to influence the content of the material in a manner favourable to its own interests. It was possible for a company to sponsor material which mentioned its own products and not be liable under the Code for its content, but only if it had been a strictly arm's length arrangement with no input by the company and no use by the company of the material for promotional purposes. Factors which might mean there had not been a strictly arm's length arrangement would include, *inter alia*, selection of the author by the pharmaceutical company.

The Panel noted that Chiesi had suggested the author for the article that appeared on the front page of the journal at issue. The Panel considered that Chiesi thus could not take the benefit of an arm's length agreement in this case, and was responsible for the article's content under the Code. The article provided details of Fostair clinical trials in COPD, which was not within the terms of the marketing authorization for the medicine. An image was also included with the caption 'Beclometasone dipropionate (BDP) crystals. BDP in combination with formoterol is available as Fostair, one of several combination inhalers on the market'.

The Panel considered that the Spring edition of Respiratory Disease in Practice was not in accordance with Fostair's marketing authorization. The undertaking given in Case AUTH/2379/1/11 was that use of the journal in question and any similar material, if not already discontinued or no longer in use, would cease forthwith. The Panel considered that this undertaking had not been complied with and ruled a breach of Clause 25. High standards had not been maintained and the Panel ruled a breach of Clause 9.1. By not complying with the undertaking given in Case AUTH/2379/1/11, Chiesi had brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

3 Alleged breach of Clauses 2 and 9.1

COMPLAINT

GlaxoSmithKline stated that it was deeply concerned over Chiesi's apparent lack of understanding as to the scope of the Code and the company's apparent unwillingness to abide by the spirit of the Code. These concerns were particularly heightened as it had recently been ruled in breach of Clauses 2, 3.2, 7.2, 7.10, 9.1 and 18.4 of the Code in Cases AUTH/2379/1/11 and AUTH/2352/8/10. GlaxoSmithKline welcomed the PMCPA's involvement at this stage following the failure of inter-company dialogue, and sought the Authority's views on what immediate action might be possible to stop on-going recurring breaches of the Code whilst this complaint was being processed. GlaxoSmithKline

alleged that all these activities taken together did not maintain the high standards expected from a pharmaceutical company (breach of Clause 9.1) and indeed brought the industry into disrepute (breach of Clause 2).

RESPONSE

Chiesi did not address specifically GlaxoSmithKline's allegations of a breach of Clauses 9.1 and 2.

PANEL RULING

The Panel noted that GlaxoSmithKline referred to two previous cases where Chiesi had been ruled in breach of the Code. Case AUTH/2379/1/11 was described at point 1 above and resulted in a ruling of a breach of Clauses 3.2, 7.2, and 7.10. Case AUTH/2352/8/10 concerned a clinical support service which was ruled to be a switch service, in breach of Clause 18.4. A breach of Clauses 9.1 and 2 was also ruled.

The Panel noted that GlaxoSmithKline's allegation of a breach of Clauses 9.1 and 2 was in relation to a pattern of behaviour as evidenced by Chiesi's conduct in this case, Case AUTH/2435/8/11 and both previous cases. Although all three cases were relatively recent and in relation to activity in the same therapy area, Case AUTH/2352/8/10 related to the provision of a medical and educational service that was linked to a particular product, not the promotion of a product outside of its marketing authorization. Case AUTH/2379/1/11 and the present case, however, both related to the promotion of Fostair outside of its marketing authorization. The Panel considered that repeated breaches of the Code in the same therapy area was a serious matter. Nonetheless, the Panel considered that the discrete rulings of breaches of Clause 2, which was reserved to indicate particular censure, in Case AUTH/2352/8/10 and the present case, Case AUTH/2435/8/11 adequately covered this allegation. The Panel did not consider that the cumulative effect of these cases was such as to warrant additional censure. No further breach of Clauses 9.1 or 2 was ruled.

The Panel was very concerned that following the company's initial response, it had to go back to Chiesi three times in order to obtain all the relevant information required to make its rulings. Responses dated 17 October and 28 September in relation to the invitation of UK health professionals to the symposium at issue revealed that UK staff had been briefed to encourage UK health professionals to attend. This contradicted the company's initial response dated 13 September that UK health professionals attended the symposium at their own wish and not through any Chiesi activity. With regard to the article in Respiratory Disease in Practice it was only when the Panel had asked twice for further information regarding its involvement that the company stated that it had suggested the author. This was unacceptable; self regulation relied upon a full and frank disclosure of the facts at the outset. The Panel considered that Chiesi's conduct in relation to this case warranted consideration by the Code of Practice Appeal Board and it decided to report the company to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to consider whether further sanctions were warranted.

COMMENTS FROM CHIESI ON THE REPORT

Chiesi was extremely concerned that, in the Panel's view it was unwilling to abide by the spirit of the Code. Chiesi took compliance with the Code extremely seriously. Chiesi had, however, been managing some circumstances that were relevant to this case. In addition it had acted recently, prior to the ruling, to address some of the issues raised in the complaint.

The inconsistencies seen in the responses in the recent case were extremely unfortunate. They were, however, not driven by an unwillingness to disclose information to the Panel but as a result of using different consultancy resources whilst recruiting new staff. Chiesi considered that it had demonstrated its willingness to give a full and frank disclosure by providing documents that were not requested, such as the presentation slides from the ATS symposium.

Chiesi submitted that GlaxoSmithKline's complaint implied that there was a concerted plan to promote Fostair in COPD; this was not the case. The symposium at the ATS was conducted entirely by the Chiesi corporate team. Chiesi Ltd (the UK affiliate) had informally invited health professionals to the symposium in good faith that the symposium did not promote Fostair outside of its licence. No information from the corporate team gave any insight into the content of the symposium. Chiesi admitted that this was an error on its part – it should have sought to clarify the content of the symposium.

The Panel had ruled a breach of undertaking in relation to Case AUTH/2379/1/11 due to the activity conducted at the ATS. There was, however, no link in the activities between the current case (Case AUTH/2435/8/11) and Case AUTH/2379/1/11. They were conducted in complete isolation from one another and Chiesi now realised that this was its failing. In respect of the ruling in Case AUTH/2379/1/11 Chiesi only considered the activities of the UK affiliate and not those of the broader Chiesi group.

Chiesi submitted that with respect to the Spring edition of Respiratory Disease in Practice, the relationship with the publishers was managed within the marketing department and not the medical department and although this was not a cause of the issues the company realised that it was not appropriate. All such activities and relationships of sponsorship now sat within the medical department and the company no longer sponsored Respiratory Disease in Practice.

Chiesi stated that prior to the ruling it had already made significant steps to resolve the issues raised by the case. Chiesi had recruited new individuals and organised refresher training on the Code. Chiesi had also acted to ensure that the Chiesi corporate team did not conduct any activities that promoted Fostair in COPD. When Chiesi received the complaint in relation to this case, it immediately shared it with the corporate team to ensure that there was no mention of scientific data on COPD at the corporate symposium at the ERS delivered on 27 September.

Chiesi reiterated that it took compliance with the Code extremely seriously. A number of factors had

contributed to the recent complaints but significant steps and corrective action had been taken to ensure that the related issues were addressed and would continue to be so.

At the consideration of the report the representatives from Chiesi acknowledged that failings had occurred resulting in conflicting submissions to the Panel. The first response to the Panel dated 13 September was written by an external consultant. The company representatives who attended for the consideration of the report were unsure what investigation the consultant undertook in compiling the response to the complaint. The subsequent responses were written by the new medical director after investigation in response to requests by the Panel.

The Chiesi representatives submitted that actions had already been put in place to address the issues raised in this case. Regular meetings with Chiesi corporate had been set up and there was good communication on the requirements of the Code to ensure that Chiesi corporate were compliant and did not put Chiesi UK at risk. Complaints would be shared with medical and marketing to provide input in to the response. Outcomes of cases were now shared with medical and marketing and other appropriate staff to ensure understanding and compliance. There had been a review of all standard operating procedures and processes. All key staff were due to undergo refresher training on the Code. Meetings with GlaxoSmithKline had been established to discuss respective concerns.

APPEAL BOARD CONSIDERATION

The Appeal Board noted that Chiesi had accepted that it had made errors and that it had taken action to improve its processes to avoid similar errors. A new medical director had been appointed.

Nonetheless, the Appeal Board was very concerned at the number of requests the Panel had had to make to obtain all of the relevant information and the fact that the incomplete and thus misleading initial response was signed and therefore agreed by the managing director. There had been three further requests from the Panel.

The Appeal Board considered that it was vital that responses to the Authority were comprehensive and not misleading by omission. The failure to provide complete and accurate information was unacceptable. The Authority and the complaints procedure, relied upon companies providing a comprehensive account of the matter in question and offering all of the relevant information even if it had not specifically been requested. In that regard the Appeal Board considered that Chiesi's provision of the slides from the ATS symposium was only to be expected. The Appeal Board decided that Chiesi should be publicly reprimanded for its failure to provide comprehensive information at the outset. It also decided in accordance with Paragraph 11.3 of the Constitution and Procedure, to require an audit of Chiesi's procedures in relation to the Code to be carried out by the Authority. The audit should be conducted in March 2012. On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary.

FURTHER CONSIDERATION BY THE APPEAL BOARD

The Appeal Board considered that the March 2012 report showed that Chiesi's procedures were not satisfactory. The Appeal Board noted that since the audit new staff were to be appointed. The Appeal Board decided that Chiesi should be re-audited in six months time. Upon receipt of the report for that audit, it would decide whether further sanctions were necessary.

Upon receipt of the October 2012 audit report, the Appeal Board noted that there had been progress since the last audit. The Appeal Board noted that in its comments upon the audit report Chiesi had stated that in addressing the PMCPA's comments about its standard operating procedures (SOPs) it could give the PMCPA a new set of SOPs within four weeks. The Appeal Board thus decided that the PMCPA should examine the revised SOPs and report its findings at the Appeal Board meeting in January 2013. The Appeal Board noted that, providing the revised SOPs were satisfactory, it would be minded to require no further sanctions.

At its meeting in January 2013 the Appeal Board noted from the PMCPA's subsequent review of Chiesi's updated SOPs that although there were still some issues to address, sufficient progress had been made and on the basis that this was maintained, no further action was required.

Complaint received	**30 August 2011**
Undertaking received	**9 November 2011**
Appeal Board consideration	**7 December 2011** **19 April 2012** **15 November 2012** **10 January 2013**
Interim case report first published	**12 June 2012**
Case completed	**10 January 2013**

CASE AUTH/2509/6/12

ANONYMOUS v ROCHE

Conduct of employees

An anonymous and uncontactable complainant alleged that employees of Roche Products had behaved inappropriately whilst attending an overseas medical conference in 2012.

The complainant stated that it seemed that Roche had lost touch with good ethics of late and had brought the industry into disrepute.

The complainant alleged that on the Saturday evening of the conference he witnessed first hand hospitality to an excess that he had rarely seen since his days as a house doctor. Whilst enjoying late night drinks at a traditional nightspot the complainant stated that he watched as two very senior Roche personnel supplied round after round of shot drinks to their delegation of doctors. He alleged that vodka shots and shots of varying colours flowed like hot lava, unstoppably. Further that two named Roche employees revelled way after midnight with a large group of customers. The group swelled in size as others joined and the party was raucous. In the complainant's view this was not good for doctors who were at a scientific meeting to be educated, nor was it good for the reputation of the pharmaceutical industry.

The complainant alleged that unfortunately one employee, who was known in the relevant medical community, proceeded to jump onto the stage drunk and that in a gesture of defiance he made a buffoon of himself by being physically evicted by door staff. The complainant considered this unacceptable behaviour outside of a scientific meeting.

The complainant expected that if the Authority examined the expense receipts/credit card statements of the two named employees, it would be surprised at the excessive levels of alcohol purchased and the time of purchase. The two Roche employees had on this occasion been lacking in their personal codes of conduct.

The detailed response from Roche is given below.

The Panel noted the seniority and responsibilities of the two named employees. According to Roche, both had attended a Roche hosted dinner on the Saturday evening and were amongst the last to leave the restaurant at about 11.30-11.45pm. They went to a bar for a drink and 'some down time away from customers'. Nine of the sixteen Roche personnel who attended the meal, including the named employees, went to the bar. The Panel questioned the choice of venue, given Roche's submission that it was a party bar that on a Saturday night when a congress was in town would be packed and very noisy. The Panel considered that the two named Roche employees would have known that it was likely that UK health professionals attending the meeting would also be at the bar and this, according to Roche, proved to be so including at least one UK health professional who was a Roche delegate. Roche submitted, however, that there was no discussion between Roche personnel and health professionals attending the meal about which venue to visit afterwards. The Panel further noted Roche's submission that its staff did not go to the bar with any health professionals nor did they arrange to meet any there.

The Panel noted that the parties' accounts about hospitality and Roche personnel at the bar differed; it was difficult in such circumstances to determine precisely what had transpired. The Panel noted Roche's submission that the two named employees met with two Roche colleagues and others at the bar. There were some UK health professionals there and the Roche group talked to health professionals that they knew but did not buy them any drinks. The complainant referred to 'two very senior Roche personnel' supplying 'round after round' of shot drinks to customers. It was unclear whether this was a reference to the named employees, who were only referred to by the complainant subsequently, or other Roche personnel. Whilst bar receipts had been provided by Roche, these were not for 'shots' and the Panel had no evidence to indicate who had consumed the drinks in question. The complainant had the burden of proving his/her complaint on the balance of probabilities.

The Panel noted Roche's submission that it had not provided any hospitality to UK health professionals at the bar, it had not invited any to attend the bar and had not bought drinks for any health professionals who were in the bar during the time Roche staff were there. Taking all the circumstances into account, the Panel considered that the complainant had not established that Roche had provided any hospitality to UK health professionals as alleged and thus ruled no breach of the Code.

The Panel noted from the document 'Compliance & International Congress' provided by Roche that it considered congresses to be 'a highly visible activity' that required 'independent responsibility and accountability'. Roche employees were instructed to focus on business objectives, strengthen customer relationships and develop knowledge and understanding. The document referred to Roche's hospitality and subsistence policy and stated that, to ensure Roche business objectives were met, staff should not remain in the bar with customers later than 11.30pm-midnight, after which time Roche attendees should withdraw from the bar. If health professionals decided to continue drinking they must pay for themselves and Roche staff must not be present (even for only soft drinks).

The Panel noted that the two named employees had arrived at the bar at approximately 12.10am. The

arrival time of other Roche personnel was not known, nor did the Panel have details about the amount of alcohol consumed previously at the restaurant. The named employees bought three rounds of alcoholic drinks, the last being purchased at 1.13am. One of the named employees had joined a group dancing on the stage of the venue, had been escorted from the venue and was not allowed back into the bar to retrieve his jacket. According to Roche a UK health professional who was also a Roche delegate remonstrated with bar staff on the Roche employee's behalf and was asked by the employee to retrieve his jacket. The employee was back at his hotel room by 1.40am. The second more senior employee had provided him with his jacket, then returned to the bar for a further 30 minutes before going back to the hotel, arriving there at around 2.15am.

The Panel noted that the provision of hospitality and other interactions between the pharmaceutical industry and health professionals outside the formal congress proceedings at international congresses was a subject that attracted much public scrutiny and criticism. Companies should be mindful of the impression given by such interactions and ensure that when applicable such activity complied with the UK Code. Other codes might also be relevant. The Panel was very concerned about the behaviour of Roche employees at a social venue at which they knew UK health professionals were in attendance. The Panel noted its comments above about the choice of venue and the likelihood of congress delegates being in attendance. The Panel considered that it was understandable that company employees would want to wind down away from health professionals at the end of a full day at congress. However, Roche employees were in the conference city as representatives of their company for business reasons and as such they should continue to be mindful of the impression created by behaviour beyond the conference and any associated subsistence/meetings. This was particularly important when interacting with UK health professionals and especially so in a late-night social environment. The Panel noted Roche's submission that its employees were aware of the need not to behave in such a way that gave the wrong impression.

The Panel noted that the parties' accounts were similar in some respects. Given that the two named Roche employees knew that UK health professionals were at the bar and had spoken to them, the Panel questioned Roche's submission that the behaviour of the Roche employee's was appropriate. The Panel considered that once the Roche employees knew that UK health professionals were at the bar they should have been mindful of the impression created by any interaction with them and the public nature of their behaviour. The Panel queried whether a shared social environment, particularly in the early hours of the morning, could ever be appropriate. The impression given by a senior member of Roche's staff being escorted off the premises at around 1am for whatever reason whilst attending a business event was most unfortunate, particularly given general criticism about interactions between health professionals and pharmaceutical companies noted above. The Panel noted its ruling above of no breach of the Code. Nonetheless, the Panel considered that the behaviour displayed in the presence of UK health professionals amounted to a failure to maintain high standards and ruled a breach of the Code. This ruling was appealed by Roche.

The Panel was concerned that Roche had not considered its senior employees' behaviour inappropriate. However, taking all the circumstances in to account, the Panel did not consider that a breach of Clause 2, a sign of particular censure, was warranted and no breach of that clause was ruled.

The Appeal Board noted that the Roche employees had attended a dinner at a local restaurant organised for its UK customers attending the conference. At the appeal hearing Roche submitted that at the end of the dinner the employees had taken a taxi to the bar in question; no UK health professionals from the dinner accompanied them. The employees subsequently purchased several rounds of drinks using company credit cards. The Appeal Board expressed surprise at the number, frequency and timing of drinks purchased. The Appeal Board noted that the bar in question could be described as a lively, loud, party bar.

The Appeal Board noted from Roche that its employees had briefly spoken with UK health professionals at the bar and so they were aware of their presence. There was, however, no evidence that the Roche employees had invited UK health professionals or that they had bought UK health professionals any drinks.

The Appeal Board noted that shortly after dancing on the stage, the senior manager was escorted from the premises and not allowed back in. The Appeal Board noted from Roche that a UK health professional who was also a Roche delegate at the conference witnessed this and 'remonstrated with the staff that the senior manager had done nothing wrong'. The UK health professional agreed to retrieve the employee's jacket from the bar and it was subsequently brought out by the more senior Roche employee.

The Appeal Board considered that the issue was not that pharmaceutical company employees and UK health professionals were present in the bar at the same time per se. Whether this was acceptable would always depend upon the circumstances of each individual case. The Appeal Board noted its comments about some aspects of the employees' conduct. Company employees needed to be mindful of the impression created by their behaviour whenever they were on company business. In the Appeal Board's view, employees attending conferences were representing their company for the whole time that they were at the conference. The Appeal Board was particularly concerned about the removal of one employee from the premises who

had not been allowed to retrieve his own belongings and the impression created which it considered was unacceptable. The circumstances amounted to a failure to maintain high standards. The Appeal Board upheld the Panel's ruling of a breach of the Code. The appeal was thus unsuccessful.

An anonymous complainant alleged that employees of Roche Products Limited had behaved inappropriately whilst attending an overseas medical conference in 2012. The complainant, although initially contactable, subsequently became uncontactable.

COMPLAINT

The complainant alleged that Roche had lost touch with good ethics of late and had brought the industry into disrepute.

The complainant alleged that on the Saturday evening of the conference he witnessed first hand hospitality to an excess that he had rarely seen since his days as a house doctor. Whilst enjoying late night drinks at a traditional nightspot, the complainant watched as two very senior Roche personnel supplied round after round of shot drinks to their delegation of doctors. He alleged that vodka shots and shots of varying colours flowed like hot lava, unstoppably. Further that two named Roche employees revelled way after midnight with a large group of customers. The group swelled in size as others joined and the party was raucous. In the complainant's view this was not good for doctors who were at a scientific meeting to be educated, nor was it good for the reputation of the pharmaceutical industry.

Unfortunately one employee, who was a known industry person in the relevant medical community, proceeded to jump onto the piano stage drunk and that in a gesture of defiance he made a buffoon of himself by being physically evicted by door staff in front of the complainant's colleagues who were enjoying a few drinks and the ambiance of the conference city. The complainant considered this unacceptable behaviour outside of a scientific meeting, even in his youth.

The complainant expected that if the Authority examined the expense receipts/credit card statements of the two employees, it would be surprised at the excessive levels of alcohol purchased and the time of purchase.

The complainant noted that Roche had looked after him very professionally for many years and he had benefited from its kind support many times, for which he was grateful. Two named Roche employees had on this occasion been lacking in their personal codes of conduct. The company itself had not and yet again promising data had been presented which the complainant hoped would translate into clinical practice.

When writing to Roche the Authority asked it to respond in relation to Clauses 2, 9.1 and 19.1 of the Code.

RESPONSE

Roche explained that the employees named were a senior manager and his manager. The meeting in question was a premier international congress, and as a leading pharmaceutical company Roche clearly had an interest in being there.

The congress opened on a Friday and on the Saturday evening Roche hosted a dinner at a restaurant for UK customers. The two named employees and the customers at their table were amongst the last of the party to leave the restaurant at around 11.30 -11.45pm. The customers and the Roche employees then went their separate ways; the two named employees went to the bar for a drink and some down time away from customers. They did not go there with any customers and nor did they arrange to meet any there.

Roche explained that the bar was part of a chain with premises in a number of cities. The bars featured live music, dancing and were promoted as venues for bachelor parties and other celebrations. Roche provided screen shots from the website to give a flavour of what the bars were like.

The two named employees arrived at the bar at approximately 12.10am. The place was very busy and loud, and a band was playing. They met two Roche colleagues and recognised employees from other pharmaceutical companies in the crowd. There were also some UK health professionals in the bar. One of the two bought a round of drinks for himself, the other named employee, the two other Roche employees and two people from an agency that they knew and who had joined their group. This consisted of six vodka rocks, ie long drinks with mixers and not shots, which cost $60; a copy of the receipt timed at 12.22am was provided. Although the Roche group talked to health professionals that they knew they did not buy them any drinks. At 12.40am the same employee bought a round of six Bacardi rocks which also cost $60 (a copy of the receipt was provided). Again these were long drinks with mixers, not shots, and were only for the Roche and agency staff.

The same employee and one of the agency staff then went to dance. There were a lot of people dancing so they were not on their own. They danced for about 30 minutes and went back to join the others. The other named employee then bought some drinks for the Roche staff and one of the agency people consisting of one beer (for the named employee), 3 vodkas and Red Bull and another vodka on the rocks costing $53 (a copy of the receipt timed at 1.13am was provided). Again no shots were purchased and nor were any of the drinks for health professionals.

The named employee and the agency colleague went back to the dance floor which was packed. Members of the band then encouraged the dancers to get up on the stage (in fact more of a platform than a real stage), which apparently happened regularly at the bar. Thus encouraged, the named employee joined others on the stage. After a while

the band stopped playing and the dancers got down from the stage. The named employee was slow to get down and the next thing he knew he was escorted off the premises. He was not told why he was asked to leave, but was not allowed back in to collect his jacket. Not long after he was shown out, a UK health professional who was a Roche delegate remonstrated with the staff that the named employee had done nothing wrong. The named employee asked the health professional if he would retrieve his jacket for him. Shortly after the second, more senior, employee came out with the jacket. The first named employee then returned to his hotel and was back in his room by 1.40am. The other named employee went back to the bar.

Whilst the named employee was dancing the second, more senior, employee remained with the rest of the group. He did not know that the named employee had been asked to leave until informed by someone else. When he realised that the jacket had been left, he took it out to the employee and then returned to the bar and left about 30 minutes later. He believed that he got back to his hotel room at around 2.15am.

Roche submitted that both employee's categorically denied going to the bar with customers or buying customers any drinks whilst they were at the bar. They also denied buying or drinking shots, and stated that the only drinks they had at the bar were the three rounds of long drinks detailed above. Both employees were at a loss to understand how the complainant concluded that 'Vodka shots and shots of varying colours were flowing like hot lava, unstoppably', but assumed that as the bar was packed and very noisy the complainant had mistakenly thought some other people were part of the Roche group.

Roche submitted that it had been presented with no evidence to doubt the version of events provided by its employees. They were senior employees with long experience of working in the pharmaceutical sector, and they knew not to party with customers. The receipts provided showed that only three rounds of long drinks were purchased. As stated above, the bar was extremely busy and noisy and thus Roche assumed that the complainant thought that other people drinking shots were part of the Roche group. Roche noted that the impression that the complainant gave of the bar as somewhere to go for a quiet drink was far from reality.

Roche noted that the complainant had alleged that its employees had 'revelled way after midnight', and that their party 'swelled in size' and was 'raucous'. This implied that they were there all night, and that they were part of a large group that stuck out from the crowd by their loud behaviour. As stated above, the two employees did not arrive until after midnight, and they also denied that they were raucous.

Roche submitted that it had no reason not to believe its employees' version of events. Roche understood that the whole atmosphere of the bar was very loud and noisy, and it queried how it was possible to single out one particular group in somewhere so crowded and which contained several hundred people crammed into the bar area.

Roche noted that the complainant had alleged that its named employee 'proceeded to jump onto the piano stage drunk', and that 'In a gesture of defiance he made a buffoon of himself by being physically evicted'. As noted above the person concerned acknowledged that he was on the stage, but that was along with other people at the invitation of the band. He also acknowledged that he was escorted off the premises, but as he was not told why he assumed that because he was slow to get off the stage the bar staff thought that he was going to cause trouble.

Roche submitted that the complainant's version of events was at variance with its employee's version. Also, the other named employee confirmed that the person concerned was not drunk. Additionally, the person concerned stated that a UK health professional, who had seen what had gone on, told the door staff that he had not done anything wrong. Roche submitted that it had not been presented with any evidence to lead it to doubt the employees' version of events. It might be that the complainant only saw the employee on the stage after the dancing had stopped and the other dancers had got down, and he thus assumed that the employee had jumped up alone, but Roche did not know why he concluded that this was 'a gesture of defiance'.

Roche concluded that the complainant had produced no evidence to substantiate his allegations as to what happened at the bar. His allegations were diametrically opposed to what Roche was told during the course of its investigation, and were contradicted by the evidence of the bar receipts. Roche's employees strongly denied buying drinks for customers or otherwise acting inappropriately. The only drinks they purchased at the bar were the three rounds of long drinks detailed in the receipts that were bought for Roche and agency staff. There was certainly not '… round after round of … vodka shots and shots of varying colours ... flowing like hot lava, unstoppably'. The website of the bar described a party bar that on a Saturday night when there was a major congress in town would be packed and very noisy, and thus it would be very difficult for anyone to clearly tell what others were doing. Roche's employees were experienced pharma staff who knew that it was not acceptable to entertain health professionals as alleged by the complainant.

Based upon its investigations, Roche submitted that there was no breach of Clause 19.1, and consequently no breach of Clauses 9.1 or 2.

In response to a request for further information by the Panel, Roche identified the Roche personnel who attended the meal on the Saturday evening. No agencies attended the dinner and Roche did not have any agency staff attending the conference.

Roche stated that there was no discussion between Roche personnel and the health professionals attending the meal about which venue to visit after the meal.

Roche submitted that, including the named employees, nine Roche personnel went to the bar. No agency staff attended as there were none at the conference (the two agency staff referred to previously by Roche were not attending the conference on behalf of Roche, although they were known to the named employee). No health professionals attended the bar at the express invitation of Roche personnel. It was not known whether any health professionals who attended the meal went to the bar without any invitation, although as mentioned previously the bar was very crowded on the night in question. The named employees spoke to some health professionals they knew.

Roche stated that the only drinks purchased by the named employees were those mentioned previously. A different Roche employee purchased two drinks for Roche personnel at a cost of $41 (copy of the receipt was provided). Another Roche employee purchased drinks for herself and six Roche colleagues at 2.19am at a cost of $139 including tip. At 2.23am the same employee purchased one drink for herself, costing $10 including tip (copies of receipts were provided). These two employees together with the personnel for whom they bought drinks were included within the nine Roche personnel referred to above. No drinks were bought for any health professionals by Roche personnel and there were no agency staff at the conference for whom Roche was responsible.

Roche submitted that there was no Roche social group in the sense of all Roche personnel being grouped together. Rather the Roche personnel were over the course of the night split into smaller groups. As the bar was very crowded it was impossible to say categorically how a third party might have perceived things. However, as the Roche personnel concerned only briefly spoke to the UK health professionals previously referred to, Roche considered it to be most unlikely that a third party would consider the UK health professionals to be part of any Roche social group and the UK health professionals themselves (who were at the bar together) would not have considered themselves to be part of the Roche social group.

As a consequence of its investigations, Roche did not regard the behaviour of the named employees inappropriate. No evidence had been produced to prove otherwise. Roche repeated that the agency staff socialised with at the bar were not Roche agency staff (although known to Roche's employees), and there were no agency staff at the conference for which Roche was responsible.

Roche submitted that its personnel were keenly aware both of the provisions of the Code regarding hospitality and of the need not to behave in such a way that gave the wrong impression. In all the circumstances Roche did not consider the behaviour of its employees to have been inappropriate and it would be willing to have the behaviour generally known.

Roche reminded the Panel that Roche was not the only pharmaceutical company whose UK personnel went to the bar that night, although it did not allege that they acted differently to Roche personnel in any way.

Roche stated that prior to attending the conference; its employees were given 'Compliance & International Congress' which provided guidance as to expected conduct.

Roche confirmed that it had not produced any internal meeting report after the conference.

PANEL RULING

The Panel noted that Clause 19.1 required that companies must not provide hospitality to members of the health professions and appropriate administrative staff except in association with scientific meetings, promotional meetings, scientific congresses and other such meetings, and training. Meetings must be held in appropriate venues conducive to the main purpose of the event. 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 supplementary information to that clause noted, *inter alia*, that the impression created by the arrangements for any meeting must always be kept in mind.

The Panel noted Roche's submission regarding the seniority and responsibilities of the two named employees. According to Roche, both had attended a Roche hosted dinner on the Saturday evening and were amongst the last of the party to leave the restaurant at about 11.30-11.45pm. They decided to go to the bar for a drink and 'some down time away from customers'. Nine of the sixteen Roche personnel who attended the meal, including the named employees also went to the bar. The Panel questioned the choice of venue, given Roche's submission that it was a party bar that on a Saturday night when congress was in town would be packed and very noisy. The Panel considered that the named employees would have known that it was likely that UK health professionals attending the conference would also be at the bar and this, according to Roche, proved to be so including at least one UK health professional who was a Roche delegate. Roche submitted, however, that there was no discussion between Roche personnel and health professionals attending the meal about which venue to visit afterwards. The Panel further noted Roche's submission that its staff did not go to the bar with any health professionals nor did they arrange to meet any there.

The Panel noted that the parties' accounts about hospitality and Roche personnel at the bar differed; it was difficult in such circumstances to determine precisely what had transpired. The Panel noted Roche's

submission that the named employees met two Roche colleagues and others at the bar. There were some UK health professionals there and the Roche group talked to health professionals that they knew but did not buy them any drinks. The complainant referred to 'two very senior Roche personnel' supplying 'round after round' of shot drinks to customers. It was unclear whether this was a reference to the named employees, who were only referred to by the complainant subsequently, or other Roche personnel. Whilst bar receipts had been provided by Roche, these were not for 'shots' and the Panel had no evidence to indicate who had consumed the drinks in question. The complainant had the burden of proving his/her complaint on the balance of probabilities.

The Panel noted Roche's submission that it had not provided any hospitality to UK health professionals at the bar, it had not invited any to attend the bar and had not bought drinks for any health professionals who were in the bar whilst Roche staff were there. Taking all the circumstances into account, the Panel considered that the complainant had not established that Roche had provided any hospitality to UK health professionals as alleged and thus ruled no breach of Clause 19.1.

The Panel noted from the document 'Compliance & International Congress' provided by Roche that it considered congresses to be 'a highly visible activity' that required 'independent responsibility and accountability'. Roche employees were instructed to focus on business objectives, strengthen customer relationships and develop knowledge and understanding. The document referred to Roche's hospitality and subsistence policy and stated that, to ensure Roche business objectives were met, staff should not remain in the bar with customers later than 11.30pm-midnight, after which time Roche attendees should withdraw from the bar. If health professionals decided to continue drinking they must pay for themselves and Roche staff must not be present (even for only soft drinks).

The Panel noted that the two named employees had arrived at the bar at approximately 12.10am. The arrival time of other Roche personnel was not known, nor did the Panel have details about the amount of alcohol consumed previously at the restaurant. One of the named employees bought three rounds of alcoholic drinks, the last being purchased at 1.13am. The named employees had joined a group dancing on the stage of the venue, had been escorted from the venue and was not allowed back into the bar to retrieve his jacket. According to Roche a UK health professional who was also a Roche delegate remonstrated with bar staff on the Roche employee's behalf and was asked by him to retrieve his jacket. This employee was back at his hotel room by 1.40am. The other named employee had provided him with his jacket, then returned to the bar for a further 30 minutes before leaving to go back to his hotel, which he reached at around 2.15am.

The Panel noted that the provision of hospitality and other interactions between the pharmaceutical industry and health professionals outside the formal congress proceedings at international congresses was a subject that attracted much public scrutiny and criticism. Companies should be mindful of the impression given by such interactions and ensure that when applicable such activity complied with the UK Code. Other codes might also be relevant. The Panel was very concerned about the behaviour of Roche employees at a social venue at which they knew UK health professionals were in attendance. The Panel noted its comments above about the choice of venue and the likelihood of congress delegates being in attendance. The Panel considered that it was understandable that company employees would want to wind down away from health professionals at the end of a full day at congress. However, Roche employees were in the conference city as representatives of their company for business reasons and as such they should continue to be mindful of the impression created by behaviour beyond the conference and any associated subsistence/meetings. This was particularly important when interacting with UK health professionals and especially so in a late-night social environment. The Panel noted Roche's submission that its employees were aware of the need not to behave in such a way that gave the wrong impression.

The Panel noted that the parties' accounts were similar in some respects. Given that the two named Roche employees knew that UK health professionals were at the bar and had spoken to them, the Panel questioned Roche's submission that the behaviour of these employees was appropriate. The Panel considered that once the Roche employees knew that UK health professionals were at the bar they should have been mindful of the impression created by any interaction with them and the public nature of their behaviour. The Panel queried whether a shared social environment, particularly in the early hours of the morning, could ever be appropriate. The impression given by a senior member of Roche staff being escorted off the premises at around 1am for whatever reason whilst attending a business event was most unfortunate, particularly given general criticism about interactions between health professionals and pharmaceutical companies noted above. The Panel noted its ruling above of no breach of Clause 19.1. Nonetheless, the Panel considered that the behaviour displayed in the presence of UK health professionals amounted to a failure to maintain high standards and ruled a breach of Clause 9.1. This ruling was appealed by Roche.

The Panel was concerned that Roche had not considered its senior named employees' behaviour inappropriate. However, taking all the circumstances in to account, the Panel did not consider that a breach of Clause 2, a sign of particular censure, was warranted and no breach of that clause was ruled.

APPEAL BY ROCHE

Roche submitted that the Panel's ruling was unclear as to what behaviour it regarded as inappropriate and thus amounted to a failure to maintain high standards. Was it the very presence of Roche employees in a bar where there were also UK health professionals, even though there was no finding that the health professionals had been provided with any hospitality, and the Roche employees and the health professionals did not form part of the same social group? Or was it

that Roche's senior manager had been escorted off the premises, even though there was no evidence produced to show that his behaviour had been unseemly or inappropriate? Or was it a combination of these factors? Roche submitted that this lack of clarity made the ruling unsafe.

Roche noted that the Panel had ruled a breach of Clause 9.1 even though it ruled no breach of Clause 19.1 or indeed of any other substantive clause. This suggested that the Panel regarded Clause 9.1 as a stand alone provision designed to capture all activities and behaviour that did not fall within the remit of other clauses. Roche submitted that the way Clause 9.1 had been used in this case was wrong and amounted to an abuse of process. Nothing in the Code (including the supplementary information to Clause 9) supported the use of Clause 9.1 in this way.

Roche noted that the Panel stated that '…once the Roche employees knew that UK health professionals were at the bar they should have been mindful of the impression created by any interaction with them and the public nature of their behaviour' and that the Panel queried '… whether a shared social environment, particularly in the early hours of the morning, could ever be appropriate'.

Roche noted that there was nothing to suggest that the Roche employees were not mindful of the impression that their behaviour might create. Roche reiterated that its employees did not provide hospitality to health professionals, that there was no evidence that their behaviour was inappropriate, and the so-called interaction consisted of a brief chat with some health professionals (they were not in the same social group) in a situation where it would have been discourteous to ignore them.

Roche further noted that the Panel seemed to suggest (although it was by no means clear) that, in its view, simply being in the same bar as health professionals was in itself inappropriate behaviour. If that was the Panel's view then there was nothing, either in the letter or spirit of the Code, which per se prohibited being in the same social setting as a health professional. The Panel's view in this regard radically widened the ambit of the Code which had implications not just for pharmaceutical companies, but also for health professionals. If pharmaceutical company staff and health professionals were to be prohibited from ever being in a shared social environment then the Code needed to be amended accordingly and/or guidance issued to companies.

Roche queried that if it was to be censured for its staff simply being in the same bar as health professionals, would the Panel also consider action against the other companies whose staff were in the bar on the night in question (although they were not doing anything different to what Roche staff were doing).

Roche submitted that the Panel had not made it clear why it regarded the behaviour of the employee who had not been escorted from the premises as inappropriate. There was no evidence that he behaved inappropriately unless the Panel regarded his being in the same bar as health professionals as being inappropriate in itself (Roche referred to its comments above). The Panel's conclusion that he failed to maintain high standards was contrary to the evidence and thus perverse.

With regard to the other named senior employee, Roche noted that the Panel also stated that his behaviour was inappropriate without being clear as to how it reached that conclusion. Again, was this conclusion reached due to his being in the same bar as health professionals, and/or was it due to his being escorted off the premises? It was indeed unfortunate that he was shown the door, but there was no evidence to prove that he had done anything wrong. Indeed he strongly denied doing anything that would warrant his being shown out, and there was no evidence to substantiate the complainant's allegations that he 'proceeded to jump onto the piano stage drunk' and 'in a gesture of defiance he made a buffoon of himself'. Roche submitted that the ruling as it applied to this employee was also perverse.

Also, as regards its employee being escorted off the premises, the Panel again mentioned the interactions between health professionals and pharmaceutical companies, and Roche again made it clear that there was no interaction as such here. Roche submitted that the Panel had inappropriately interpreted the supplementary information to Clause 19.1 (the impression that was created by the arrangements for any meeting must always be kept in mind). Simply being in the same establishment as a health professional did not amount to the kind of interaction with which the supplementary information to Clause 19.1 was concerned (the supplementary information was concerned with the arrangements for any meeting). Nonetheless, Roche always expected its employees to behave appropriately whilst on company business, whether or not health professionals were present.

Roche noted that the Panel was concerned that the company had not considered that its two employees' behaviour was inappropriate. In the view of the foregoing and the evidence Roche submitted that it had been presented with there were no grounds for taking such a view, and as an employer it would be inappropriate for it to do so.

In conclusion Roche submitted that the Panel's ruling of a breach of Clause 9.1 was illogical, perverse and simply wrong. If the ruling was upheld it would have serious implications for the whole industry and for health professionals. Accordingly Roche requested the Appeal Board to rule no breach of the Code.

Upon being advised that the PMCPA could now not contact the complainant, Roche queried whether it would be fair and rational to allow the complaint to continue, and asked that it be struck out.

RESPONSE FROM THE COMPLAINANT

As the complainant was now uncontactable there were no comments upon the appeal.

APPEAL BOARD RULING

At the appeal hearing the Chairman of the Appeal Board advised Roche that he had directed the Appeal Board to note that the complainant, although initially contactable, had subsequently become uncontactable. The complainant was thus now being treated as anonymous and uncontactable.

In response to a question regarding Roche's failure to provide an itemised bill as requested by the case preparation manager, Roche stated that this had not been provided by Roche's finance department.

The Appeal Board noted that whilst Roche disputed some of the complainant's allegations there were nonetheless some similarities between the parties' submissions.

The Appeal Board noted that the Roche employees had attended a dinner at a local restaurant organised for its UK customers attending the conference. At the appeal hearing Roche submitted that at the end of the dinner the employees had taken a taxi to the bar in question; no UK health professionals from the dinner accompanied them. The employees subsequently purchased several rounds of drinks using company credit cards. The Appeal Board expressed surprise at the number, frequency and timing of drinks purchased. The Appeal Board noted that the bar in question could be described as a lively, loud, party bar.

The Appeal Board noted from Roche that its employees had briefly spoken with UK health professionals at the bar and so they were aware of their presence. There was, however, no evidence that the Roche employees had invited UK health professionals or that they had bought UK health professionals any drinks.

The Appeal Board noted that shortly after dancing on the stage, one of the senior named employees was escorted from the premises and not allowed back in. The Appeal Board noted from Roche that a UK health professional who was also a Roche delegate at the conference witnessed this and remonstrated with the staff that the employee had done nothing wrong. The UK health professional agreed to retrieve the employee's jacket from the bar and it was subsequently brought out by the second, more senior employee.

The Appeal Board considered that the issue was not that pharmaceutical company employees and UK health professionals were present in the bar at the same time per se. Whether this was acceptable would always depend upon the circumstances of each individual case. The Appeal Board noted its comments about some aspects of the employees' conduct. Company employees needed to be mindful of the impression created by their behaviour whenever they were on company business. In the Appeal Board's view, employees attending conferences were representing their company for the whole time that they were at the conference. The Appeal Board was particularly concerned about the removal of one employee from the premises who had not been allowed to retrieve his own belongings and the impression created which it considered was unacceptable. The circumstances amounted to a failure to maintain high standards. The Appeal Board upheld the Panel's ruling of a breach of Clause 9.1. The appeal was thus unsuccessful.

Complaint received	**4 June 2012**
Case completed	**7 November 2012**

ALLERGAN/DIRECTOR v MERZ

Alleged breach of undertaking

Allergan complained about the promotion of Bocouture (botulinum toxin type A) by Merz Pharma UK at the FACE Conference and Exhibition, in June 2012. The materials at issue were the Merz exhibition stand and a leavepiece. As the complaint involved an alleged breach of undertaking, it was taken up by the Director without the need for prior inter-company dialogue, as it was the Authority's responsibility to ensure compliance with undertakings. Allergan supplied Botox (botulinum toxin type A).

The exhibition stand, headed 'Merz Aesthetics, Your partner in facial aesthetics', featured a photograph of a vial of Bocouture and a vial of Botox side-by-side. To the right of the photograph was the claim 'According to comparative clinical studies [Sattler *et al* 2010] Bocouture vs Botox: Comparable efficacy, 1:1 Clinical Conversion Ratio'. Below the photograph, in less prominent font, was the statement 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of botulinum toxin' which was referenced to the Bocouture summary of product characteristics (SPC), March 2012. Below a thick, blue horizontal line was reference to Bocouture's use in the temporary improvement of moderate to severe glabellar frown lines. The front cover of the leavepiece was similar to the exhibition stand.

Allergan alleged that the items at issue and overall campaign had clearly been designed to lead the prescriber to conclude that Bocouture and Botox were interchangeable in terms of potency units and that they delivered equivalent results in clinical practice.

Allergan considered that the visual was clearly designed to emphasise a direct 1:1 equivalence/conversion of the two products and the overall message taken away by a health professional was that Bocouture and Botox were equally potent and could be converted at a ratio of 1:1.

The current Bocouture summary of product characteristics (SPC) (updated on 6 March 2012) stated: 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of Botulinum toxin'. There was no reference to equal potency. The Xeomin 50U SPC still contained information regarding its non-inferiority studies (in Section 5.1, Pharmacodynamic properties) but this was in relation to patients with blepharospasm or cervical dystonia. Non-inferiority studies did not support claims of equivalence. The SPC for Botox 50, 100 and 200 units stated: 'Botulinum toxin units are not interchangeable from one product to another. Doses recommended in Allergan units are different from other botulinum toxin preparations'.

Allergan submitted that the promotion by Merz of this 1:1 clinical conversion ratio between Bocouture and Botox was of significant concern. No 'dosing conversion' occurred or should be implied from the non-inferiority study conducted by Merz (Sattler *et al*). The direct medical impact was that a significant patient safety risk existed with prescribers encouraged to transfer information from one label to another product.

Allergan noted the ruling in Case AUTH/2270/10/09 that the results of a non-inferiority study could not be used to claim equivalence. Merz's submission in that case was that it had no data to support a claim that Xeomin was equivalent to Botox. Allergan considered this was still so, Merz had not published any new clinical data that supported a claim of equivalence for either Xeomin or Bocouture. Therefore, Allergan alleged the visuals which implied equivalence/equipotency and the claim of a '1:1 Clinical Conversion Ratio' between Bocouture and Botox (ie equivalence) were a breach of the undertaking given in Case AUTH/2270/10/09.

The detailed response from Merz is given below.

The Panel noted that Case AUTH/2270/10/09 concerned a complaint from Allergan that Merz's claim that Xeomin was 'At least as effective as Botox with a similar safety profile' without appropriate context and qualification did not accurately reflect the available evidence and was misleading. Allergan had submitted that to claim 'At least as effective as', Merz needed further evidence to confirm equivalent efficacy and clinically relevant superiority. The claim at issue was referenced to two non-inferiority studies. The Panel had considered that there was a difference between showing non-inferiority and showing comparability and that the claim that Xeomin was 'At least as effective as Botox' did not reflect the available evidence. It implied possible superiority of Xeomin and was misleading as alleged and breaches of the Code were ruled. Following an appeal by Merz, the Appeal Board noted Merz's submission that it had no data upon which to claim that Xeomin was equivalent to Botox. The Appeal Board's view was that the claim 'At least as effective as' not only implied equivalence but also possible superiority which was misleading. The claim could not be substantiated by the available data and the Panel's rulings were upheld.

The Panel noted that there was still no data to show whether Bocouture/Xeomin was equivalent to Botox/Vistabel. As when the ruling in Case AUTH/2270/10/09 was made, there were still only non-inferiority studies which showed that the medicines were no worse than each other by a clinically acceptable pre-specified margin.

Turning to the present case, the Panel noted that the material now at issue was different to that at issue in Case AUTH/2270/10/09 where the comparison at issue had been between Xeomin and Botox; the comparison now at issue was between Bocouture and Botox. Bocouture and Xeomin, however, were the same product but with different indications.

The Panel did not agree with Allergan's position that the materials in question implied that Bocouture and Botox were equivalent in clinical practice. The Panel considered that the material at issue was very different to that at issue in Case AUTH/2270/10/09 which featured the claim, 'At least as effective as Botox with a similar safety profile'.

The Panel noted that, for the temporary improvement of moderate to severe glabellar frown lines, the initial dose for both Bocouture and Botox was 20U. Sattler *et al* compared the effect of 24 units of each medicine in the treatment of glabellar frown lines and showed that Bocouture was non-inferior to Botox. The materials now at issue featured the reasonably prominent claim 'Comparable efficacy' which in the opinion of the Panel meant that neither the bullet point that followed, '1:1 Clinical Conversion Ratio', nor the depiction of the adjacent vials implied equipotence or clinical equivalence as alleged. Given the common understanding of 'comparable' the Panel did not consider that the materials were caught by the undertaking given in Case AUTH/2270/10/09 which applied to claims of equivalence and possible superiority. The Panel thus ruled no breaches of the Code including Clause 2. These rulings were unsuccessfully appealed by Allergan.

Allergan Limited complained about the promotion of Bocouture (botulinum toxin type A) by Merz Pharma UK Ltd at the FACE Conference and Exhibition, in June 2012. The materials at issue were the Merz exhibition stand (ref 1149/MER/MAY/2012/JH) and a leavepiece (ref 1080/BOC/FEB/2012/JH) given to delegates. As the complaint involved an alleged breach of undertaking, it was taken up by the Director without the need for prior inter-company dialogue, as it was the Authority's responsibility to ensure compliance with undertakings. Allergan supplied Botox (botulinum toxin type A).

The exhibition stand, headed 'Merz Aesthetics, Your partner in facial aesthetics', featured a photograph of a vial of Bocouture and a vial of Botox side-by-side. To the right of the photograph was the claim 'According to comparative clinical studies [Sattler *et al* 2010] Bocouture vs Botox: Comparable efficacy, 1:1 Clinical Conversion Ratio'. Below the photograph, in small font, was the statement 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of botulinum toxin' which was referenced to the Bocouture summary of product characteristics (SPC), March 2012. Below a thick, blue horizontal line was reference to Bocouture's use in the temporary improvement of moderate to severe glabellar frown lines.

The front cover of the leavepiece had the same heading as the exhibition stand and similarly featured a photograph of a vial of Bocouture and a vial of Botox, side-by-side and the claim as stated above referenced to Sattler *et al*. Below the photograph was a thick blue horizontal line and beneath that was the statement as above referenced to the Bocouture SPC, February 2012 together with reference to Bocouture's use in the temporary improvement of moderate to severe glabellar frown lines.

COMPLAINT

Allergan alleged that the items at issue and overall campaign had clearly been designed to lead the prescriber to conclude that Bocouture and Botox were interchangeable in terms of potency units and that they delivered equivalent results in clinical practice.

Allergan noted that Merz had used the claim '1:1 Clinical Conversion Ratio' alongside a visual of a Bocouture and Botox vial standing side-by-side. The visual was clearly designed to emphasise a direct 1:1 equivalence/conversion of the two products. The claim 'According to comparative clinical studies' was included. Less prominently and in smaller font was the statement 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of Botulinum toxin' taken from the Bocouture SPC.

Allergan considered that the overall message taken away by a health professional was that Bocouture and Botox were equally potent and could be converted at a ratio of 1:1.

The current Bocouture SPC (updated on 6 March 2012) stated:

> 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of Botulinum toxin'.

Allergan stated that the UK Bocouture SPC (and that of Merz's product Xeomin 50U (botulinum toxin type A)) was changed following Allergan's communication to the Pharmacovigilance Working Party (PhVWP) highlighting the potential patient safety concerns with wording in the Bocouture 50U and Xeomin 50U SPCs. In the Bocouture SPC any reference to equal potency had been removed.

Allergan further stated that the statement regarding 1:1 dosing ratio in Section 4.2 of the Xeomin 50U SPC, Posology and method of administration, had been removed. The Xeomin 50U SPC still contained information regarding its non-inferiority studies (in Section 5.1, Pharmacodynamic properties) but this was in relation to patients with blepharospasm or cervical dystonia. As previously established, non-inferiority studies did not support claims of equivalence.

The SPC for Botox 50, 100 and 200 units stated:

> 'Botulinum toxin units are not interchangeable from one product to another. Doses recommended in Allergan units are different from other botulinum toxin preparations'.

Allergan submitted that the promotion by Merz of this 1:1 clinical conversion ratio between Bocouture and Botox was of significant concern. No 'dosing conversion' occurred or should be implied from the non-inferiority study conducted by Merz with its toxin (Sattler *et al*). The direct medical impact was that a significant patient safety risk existed with prescribers encouraged to transfer information from one label to another product.

Allergan noted that the PMCPA ruled in Case AUTH/2270/10/09 that the results of a non-inferiority study could not be used to claim equivalence. Merz's own submission in that case was that it had no data to support a claim that Xeomin was equivalent to Botox. Allergan considered this was still the case and Merz had not published any new clinical data that supported a claim of equivalence for either Xeomin or Bocouture. Therefore, Allergan considered the visuals which implied equivalence/equipotency and the claim of a '1:1 Clinical Conversion Ratio' between Bocouture and Botox (ie equivalence) were a breach of the undertaking given in Case AUTH/2270/10/09 and as such were in breach of Clause 25.

RESPONSE

Merz noted that in Case AUTH/2270/10/09 it was found in breach of the Code for claiming that Xeomin was 'At least as effective as Botox with a similar safety profile'. The Panel considered that the claim implied possible superiority of Xeomin vs Botox which was not supported by the available data. The breach was upheld upon appeal.

Merz submitted that Bocouture had been demonstrated to have similar efficacy and tolerability to Botox when used with a 1:1 dosing conversion ratio. The use of non-inferiority studies to make this point, (specifically that of similar efficacy at a fixed dosing ratio), had been reviewed by the Panel in Case AUTH/2357/9/10 regarding the promotion of Pradaxa. The Panel ruled that the claim '…efficacy and safety comparable to…' was substantiated by the non-inferiority studies referenced. This was taken to appeal and the Appeal Board further reinforced that comparable did not imply equivalence. Merz did not consider that the term used in the exhibition panel or leavepiece now at issue (ie comparable efficacy) was interchangeable with or implied equivalence which, as previously established, was not a general term but had a very specific meaning. As such Merz considered these claims were sufficiently different to the original case not to be considered a breach of Clause 25.

Furthermore Merz noted that in Case AUTH/2496/4/12, claims of 'Equipotent' or 'Equal Potency' were ruled on by the Panel in the context of Case AUTH/2270/10/09 and no breach of Clause 25 was found. The term, 'comparable' conferred even less likelihood of implied superiority than 'equipotent'.

Merz submitted that subsequent to these rulings, two articles about the use of toxins in clinical practice had been published recently in peer reviewed publications (Jandhyala 2012 and Prager *et al* 2012). Both studies compared the authors' up-to-date experiences of using Botox and Bocouture in a large number of patients. The authors' conclusions were consistent with the claims of comparable efficacy. Merz therefore considered that the items in question were also not in breach of Clauses 9.1 or 2.

Finally, Merz submitted that the material at issue had already been withdrawn following an internal review of promotional material based on the undertaking (signed 27 June 2012) to comply with the Panel's ruling in Case AUTH/2496/4/12.

PANEL RULING

The Panel noted that Case AUTH/2270/10/09, concerned a complaint from Allergan that the claim by Merz that Xeomin was 'At least as effective as Botox with a similar safety profile' without appropriate context and qualification did not accurately reflect the available evidence and was misleading. Allergan had submitted that to make the claim 'At least as effective as', Merz needed further evidence to confirm equivalent efficacy and clinically relevant superiority. The claim at issue was referenced to Benecke *et al* (2005) and Roggenkamper *et al* (2006) both of which were non-inferiority studies. The Panel had considered that there was a difference between showing non-inferiority and showing comparability and that the claim that Xeomin was 'At least as effective as Botox' did not reflect the available evidence. It implied possible superiority of Xeomin and was misleading as alleged and breaches of the Code were ruled. Following an appeal by Merz, the Appeal Board noted Merz's submission that it had no data upon which to claim that Xeomin was equivalent to Botox. The Appeal Board stated that in its view, the claim 'At least as effective as' not only implied equivalence but also possible superiority which was misleading. The Appeal Board did not consider that the claim could be substantiated by the available data and the Panel's rulings were upheld.

The Panel noted that there was still no data to show whether Bocouture/Xeomin was equivalent to Botox/Vistabel. As when the ruling in Case AUTH/2270/10/09 was made, there were still only non-inferiority studies which showed that the medicines were no worse than each other by a clinically acceptable pre-specified margin.

Turning to the present case, the Panel noted that the material now at issue was different to that at issue in Case AUTH/2270/10/09. In Case AUTH/2270/10/09 the comparison at issue had been between Xeomin and Botox; the comparison now at issue was between Bocouture and Botox. Bocouture and Xeomin, however, were the same product but with different indications – Bocouture was indicated for the temporary improvement in the appearance of glabellar frown lines whilst Xeomin was for the symptomatic treatment of blepharospasm, cervical dystonia and post-stroke spasticity of the upper limb.

The Panel did not agree with Allergan's position that the materials in question implied that Bocouture and

Botox were equivalent in clinical practice. The Panel considered that the material at issue was very different to that at issue in Case AUTH/2270/10/09 which featured the claim, 'At least as effective as Botox with a similar safety profile'.

The Panel noted that, for the temporary improvement of moderate to severe glabellar frown lines, the initial dose for both Bocouture and Botox was 20U. Sattler *et al* compared the effect of 24 units of each medicine in the treatment of glabellar frown lines and showed that Bocouture was non-inferior to Botox. The materials now at issue featured the reasonably prominent claim 'Comparable efficacy' which in the opinion of the Panel meant that neither the bullet point that followed, '1:1 Clinical Conversion Ratio', nor the depiction of the adjacent vials implied equipotence or clinical equivalence as alleged. Given the common understanding of 'comparable' the Panel did not consider that the materials were caught by the undertaking given in Case AUTH/2270/10/09 which applied to claims of equivalence and possible superiority. The Panel thus ruled no breach of Clause 25. The Panel consequently ruled no breach of Clauses 9.1 and 2.

APPEAL BY ALLERGAN

Allergan appealed the Panel's ruling of no breach of Clause 25. It noted that Merz had used the claim '1:1 Clinical Conversion Ratio' alongside a visual of a Bocouture and Botox vial standing side-by-side which it considered clearly emphasised a direct 1:1 equivalence/conversion of the two products. The phrase 'According to comparative clinical studies' was included, as well as the statement 'Comparable efficacy'. Less prominently and in smaller font was the SPC statement 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of botulinum toxin'.

Allergan alleged that the take away message would be that the products were equivalent, interchangeable and could be converted 1:1.

The current SPC for Bocouture (which was updated on 6 March 2012) stated:

> **'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of Botulinum toxin'.**

Allergan stated that changes to the UK Bocouture and Xeomin 50U SPCs were approved after Allergan had highlighted to the PhVWP the potential patient safety concerns with the previous wording. Any reference to 'equal potency' had been removed from the Bocouture SPC.

Allergan further stated that in Section 4.2 of the Xeomin 50U SPC the statement regarding 1:1 dosing ratio had been removed; Section 5.1 still contained information regarding its non-inferiority studies but this was in relation to patients with blepharospasm or cervical dystonia. As previously established, non-inferiority studies did not support claims of equivalence.

The SPCs for Botox 50, 100 and 200 units stated:

> **'Botulinum toxin units are <u>not interchangeable from one product to another</u>. Doses recommended in Allergan units are different from other botulinum toxin preparations'.**

Allergan alleged that the promotion of a '1:1 Clinical Conversion Ratio' between Bocouture and Botox was a source of significant concern. No 'dosing conversion' occurred or should be implied from the non-inferiority study conducted by Merz with its toxin (Sattler *et al*). The direct medical impact was that a significant patient safety risk existed with prescribers encouraged to transfer information from one label to another product.

Allergan noted that the PMCPA ruled in Case AUTH/2270/10/09 that the results of a non-inferiority study could not be used to claim equivalence. Merz's submission in that case was that it had no data to support a claim that Xeomin was equivalent to Botox. As acknowledged by Merz in Case AUTH/2496/4/12, this was still the case and Merz had not published any new clinical data that supported a claim of equivalence for Bocouture (or Xeomin). Therefore, Allergan alleged that any claim which implied clinical equivalence and interchangeability must be in breach of the undertaking made in Case AUTH/2270/10/09.

Allergan alleged that the overall impression given by the materials at issue was sufficiently similar with regard to a claim for 'equivalence' to be covered by the undertaking given in Case AUTH/2270/10/09. The insertion of the 'reasonably prominent' claim 'Comparable efficacy' did not negate the overall impression given by the visual and the accompanying claim of a 1:1 clinical conversion ratio.

Allergan alleged that Merz clearly intended to convey a message of equivalence and interchangeability even though it had been clearly established that there was no new data to support this message and the updates to the Bocouture and Xeomin SPCs in March 2012. As stated by the Appeal Board in Case AUTH/2496/4/12, implying the products were clinically equivalent and hence interchangeable was contrary to statements in the SPCs and raised possible patient safety concerns.

Allergan alleged that the two recent articles cited by Merz in its response did not support a claim of clinical equivalence, as already acknowledge by Merz. Jandhyala was discussed in Case AUTH/2496/4/12; this mixed treatment comparisons meta-analysis included only one head-to-head study (Sattler *et al*).

Allergan noted that Prager *et al* was a retrospective analysis of daily practice in treatment of the upper face. 1256 patient charts were reviewed demonstrating use of the Merz toxin (88%), the Allergan toxin (10.4%) and Ipsen toxin (1.6%) in the treatment of the glabellar frown lines (48.3%), lateral periorbital wrinkles (27.4%) and/or horizontal

forehead lines (24.4%). Overall, no statistically significant differences between the Merz and Allergan products were found for any of the parameters measured. A validated patient satisfaction scale had not been used in this study, instead a yes/no assessment captured patient satisfaction. In the analysis, the data were actually pooled and analyzed as a whole under the term 'upper face'. No data was provided to show the doses administered to each region. It was inappropriate to draw conclusions on clinical efficacy when there had only been data gathered on patient satisfaction and time to re-injection.

In conclusion, Allergan submitted that the overall impression given by the materials at issue was sufficiently similar with regard to a claim for 'equivalence' to be covered by the undertaking given in Case AUTH/2270/10/09. The insertion of the 'reasonably prominent' claim 'Comparable efficacy' did not negate the overall impression given by the visual and the accompanying claim of a 1:1 clinical conversion ratio.

Allergan noted that the PMCPA had ruled in Case AUTH/2270/10/09 that the results of a non-inferiority study could not be used to claim equivalence. Merz's own submission in that case, in Case AUTH/2496/4/12 and confirmed in Case AUTH/2516/6/12, was that it had no data to support a claim that Xeomin/Bocouture was equivalent to Botox. This was still the case and Merz had not published any new clinical data that supported a claim of equivalence.

Therefore, Allergan alleged that the visuals which implied equivalence/equipotency and the claim of a '1:1 Clinical Conversion' between Bocouture and Botox (ie equivalence) breached the undertaking given in Case AUTH/2270/10/09 and were thus in breach of Clause 25.

COMMENTS FROM MERZ

Merz noted that in Case AUTH/2270/10/09 Allergan had complained about the use of the claim 'At least as effective as Botox with a similar safety profile'. The Panel had ruled that this was misleading since it implied 'possible superiority' of Xeomin vs Botox which was not supported by the available data at the time. The breach was upheld upon appeal.

Merz submitted that its consistent interpretation of the undertaking given in Case AUTH/2270/10/09 was aligned to that of the Panel, ie that it sought to ensure that there was no implied superiority in promotional campaigns and accordingly all materials were developed with this in mind. Merz took undertakings seriously and its consistent intent was to comply with this. When the Medicines and Healthcare products Regulatory Agency (MHRA) approved Bocouture (June 2010) with an SPC which stated 'equal potency' there was still no implied superiority in any Merz promotional materials. Despite very consistent promotional campaigns for Bocouture there was no challenge from the date of publication of Case AUTH/2270/10/09 (January 2010) until the complaint now in hand (15 June 2012). This therefore suggested that the interpretation of this undertaking was consistently shared not only by Merz and the Panel but also by Allergan.

Turning to the case now at issue (Case AUTH/2515/6/12) the Panel's summary was clear: 'Given the common understanding of 'comparable' the Panel did not consider that the materials were caught by the undertaking … which applied to claims of equivalence and possible superiority'.

Merz noted that the interpretation of the Case AUTH/2270/10/09 undertaking by it, the Panel (and arguably Allergan) had been recently broadened (after more than two years) in Case AUTH/2496/4/12. The Panel originally ruled no breach of the Code with regard to an alleged breach of undertaking in Case AUTH/2270/10/09 which related to comparisons between Bocouture/Xeomin and Botox/Vistabel, concluding that since there was no implied superiority it could not constitute a breach of undertaking. The ruling was appealed and the Appeal Board (July 2012) overturned the Panel ruling, stating that 'although the claim at issue was not the same as that in Case AUTH/2270/10/09, it was sufficiently similar with regard to a claim for "equivalence" for it to be covered by the undertaking previously given.' This new interpretation and the timing of it was important in the current case.

As a result of this new interpretation Merz was found in breach of Clause 2. The Code was clear that Clause 2 was a sign of particular censure and was reserved for such circumstances. Examples included (but were not limited to) '… prejudicing patient safety and/or public health, excessive hospitality, inducements to prescribe, inadequate action leading to a breach of undertaking, promotion prior to the grant of a marketing authorization, conduct of company employees/agents that falls 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'. Whilst this list was not exhaustive it did not capture any activity under review in the current case. Once the original undertaking was signed all future promotional materials were carefully developed to avoid the original interpretation of implied superiority, (ie adequate action was taken) and therefore the absolute intent of Merz was to faithfully comply with the undertaking.

Merz supported the Panel's ruling that the claim 'at least as effective as' which implied superiority was significantly different from the claims at issue which related to 'comparable efficacy'. As such this was not a breach of undertaking. Since the materials in question pre-dated the findings of Case AUTH/2496/4/12 Merz could not have knowingly breached the undertaking and therefore could not be considered to have breached Clause 9.1. Nor could this intent to faithfully comply with the undertaking be considered to bring discredit upon the pharmaceutical industry.

FINAL COMMENTS FROM ALLERGAN

Allergan noted the Panel's ruling in Case AUTH/2270/10/09 that the results of a non-inferiority study could not be used to claim equivalence. Merz's own submission in that case was that it had no data to support a claim that Xeomin was equivalent to Botox. As acknowledged by Merz in Case AUTH/2496/4/12, this was still the case and Merz had not published any new clinical data that supported a claim of equivalence for Bocouture (or Xeomin).

The ruling in Case AUTH/2270/10/09 by the Panel and then by the Appeal Board was not only in relation to an implied claim of 'superiority' as Merz continued to believe but also in relation to 'comparability' and 'equivalence'. The summary of the case made the ruling very clear as follows: 'The Panel considered that there was a difference between showing non-inferiority to showing comparability. The Panel considered on the basis of the data the claim that Xeomin was "At least as effective as Botox" did not reflect the available evidence. It implied possible superiority of Xeomin as alleged and was misleading. Breaches of the Code were ruled'. Upon appeal by Merz the Appeal Board noted that both parties agreed that Benecke *et al* and Roggenkamper *et al* were non-inferiority studies that showed that Xeomin was no worse than Botox by a pre-specified margin (delta) that was clinically acceptable. The Appeal Board noted Merz's submission that it had no data upon which to make the claim that Xeomin was equivalent to Botox. In the Appeal Board's view the claim 'At least as effective' not only implied equivalence but also possible superiority which was misleading. The Appeal Board did not consider that the claim could be substantiated by the available data. The Appeal Board upheld the Panel's ruling of breaches of the Code.

Therefore, Allergan submitted that any claim which implied clinical equivalence and interchangeability must breach the undertaking given in Case AUTH/2270/10/09.

Allergan submitted that the overall impression given by the materials at issue was sufficiently similar with regard to a claim for 'equivalence' to be covered by the undertaking given in Case AUTH/2270/10/09. The insertion of the 'reasonably prominent' claim 'Comparable efficacy' did not negate the overall impression given by the visual and the accompanying claim of a 1:1 clinical conversion ratio.

Allergan disagreed with Merz's view that the insertion of the words 'Comparable efficacy' constituted 'adequate action' to comply with the undertaking given in Case AUTH/2270/10/09 and in that regard Allergan referred to the above summary of that case where a clear distinction between non-inferiority and comparability was highlighted.

Allergan submitted that Merz clearly intended to convey a message of equivalence and interchangeability despite the fact that it had been clearly established there was no new data to support this message and despite the updates to the Bocouture and Xeomin SPCs in March 2012. As stated by the Appeal Board in Case AUTH/2496/4/12, implying the products were clinically equivalent and hence interchangeable was contrary to statements in the SPCs and raised possible patient safety concerns.

In Case AUTH/2270/10/09 the Panel ruled that the results of a non-inferiority study could not be used to claim equivalence. Merz's own submission in that case, in Case AUTH/2496/4/12 and confirmed in Case AUTH/2516/6/12, was that it had no data to support a claim that Xeomin/Bocouture was equivalent to Botox. This was still the case and Merz had not published any new clinical data that supported a claim of equivalence.

Allergan thus submitted that the visuals which implied equivalence/equipotency and the claim of a '1:1 Clinical Conversion' between Bocouture and Botox, (ie equivalence) breached the undertaking given in Case AUTH/2270/10/09 and as such were in breach of Clause 25 and consequently Clauses 9.1 and 2.

APPEAL BOARD RULING

The Appeal Board noted its ruling in Case AUTH/2270/10/09 which stated that:

> 'The Appeal Board noted Merz's submission at the appeal that it had no data upon which to make the claim that Xeomin [Bocouture] was equivalent to Botox. In the Appeal Board's view the claim 'At least as effective as' not only implied equivalence but also possible superiority which was misleading. The Appeal Board did not consider that the claim could be substantiated by the available data. The Appeal Board upheld the Panel's ruling of breaches of Clauses 7.2 and 7.3.'

The Appeal Board noted that the undertaking in that case related to claims of implied equivalence and/or superiority. The Appeal Board considered that in the case now in question, Case AUTH/2515/6/12, there was clearly no claim for implied superiority of Bocouture vs Botox. The issue to be considered was, did the material overall suggest that the two medicines were equivalent?

The Appeal Board noted that the material, which was used at an aesthetics meeting, featured the image of a vial of Bocouture and Botox side-by-side together with the claims 'Comparable efficacy' and '1:1 Clinical Conversion Ratio'. The Appeal Board noted that the study cited in support of the claims was Sattler *et al* which showed that in the treatment of glabellar lines, 24 units of each medicine produced comparable clinical results; the response rates supported the non-inferiority of Bocouture to Botox.

In the Appeal Board's view 'Comparable efficacy' did not imply equivalence. Overall the Appeal Board considered that the material at issue was sufficiently

different to that at issue in Case AUTH/2270/10/09 for it not to be covered by the undertaking given in that case. The Appeal Board upheld the Panel's ruling of no breach of Clause 25, and consequently the rulings of no breach of Clause 2 and 9.1. The appeal was thus unsuccessful.

Complaint received	**15 June 2012**
Case completed	**11 October 2012**

CLINICAL LEAD PHARMACIST v PROSTRAKAN

Conduct of representatives

A clinical lead pharmacist at a hospital NHS foundation trust, complained about the conduct of ProStrakan representatives in relation to the promotion of Abstral (fentanyl) which was indicated for the management of breakthrough pain in adults using opioid therapy for chronic cancer pain.

The complainant referred to a meeting in the urology department to discuss using Abstral in oncology patients presenting with cancers of urological origin. This was within licence as the complainant understood it. However, the discussion moved to the use of Abstral post-operatively in patients who had had urological surgery. This was outside licence although technically these patients would have had surgery for an oncological reason. The complainant was not clear who initiated this discussion but the representative did not try to extract herself from the discussion on the basis that it was an unlicensed indication and it should not be discussed.

The upshot of the meeting was that one of the attendees, a specialist nurse, contacted the acute pain team to discuss using Abstral in this way. The complainant confirmed with ProStrakan that it had no data to support this indication.

At this point the complainant became aware of the meeting. Since then he had had a meeting with the representative and her line manager. They initially contested his view of the licence and whether their product was licensed but they also apologised. However the complainant considered that a more formal acknowledgement and possible rebuke of their activities might be in order.

The detailed response from ProStrakan is given below.

The Panel noted that the issue was in relation to using Abstral post-operatively following urological surgery. In the complainant's view this was outside the licence. ProStrakan submitted that its representative had discussed the use of Abstral in patients with urological cancers undergoing surgery purely on the basis that such patients might still be subject to breakthrough pain post-operatively despite receiving other opioid treatment for chronic cancer pain. Urological surgery might be focussed on debulking tumours and/or relieving urological obstruction. In such cases the patient would still be a cancer sufferer. ProStrakan agreed with the complainant that if surgery removed the cancer the patient would not have breakthrough cancer pain.

The Panel considered that it was important that representatives were very clear about the indications for use of the products they promoted. It would be unacceptable to promote Abstral in patients who did not have cancer however there was no evidence that this had happened. The Panel considered that the complainant had not proven his case on the balance of probabilities and no breach of the Code was ruled. Consequently the Panel did not consider that the representative had failed to maintain a high standard of ethical conduct or failed to comply with the Code. No breach of the Code was ruled.

The representative's presentation included an introduction to breakthrough cancer pain. The Panel noted that the presentation did not give the full indication. The brand logo referred to breakthrough cancer pain but there was no mention that patients needed to be using opioid therapy for chronic cancer pain. The Panel considered that this would have been helpful but the absence in the particular circumstances of this case did not amount to a breach of the Code.

The Panel did not consider that the briefing material advocated a course of action likely to breach the Code and thus no breach of the Code was ruled.

Given its rulings above the Panel decided that there was no breach of Clause 2 and ruled accordingly.

A clinical lead pharmacist at a hospital NHS foundation trust, complained about the conduct of representatives of ProStrakan Ltd in relation to the promotion of Abstral (fentanyl). Abstral was indicated for the management of breakthrough pain in adults using opioid therapy for chronic cancer pain.

COMPLAINT

The complainant referred to an organised meeting within the urology department in late June to discuss using Abstral in oncology patients presenting with cancers of urological origin. This was within licence as the complainant understood it.

The meeting then began to discuss using Abstral in the post-operative phase for patients having urological surgery. This was outside licence although technically these patients would have had surgery for an oncological reason. The complainant was not clear who initiated this discussion but the company representative did not try to extract herself from the discussion on the basis that it was an unlicensed indication and it should not be discussed.

The upshot of the meeting was that one of the specialist nurses at the meeting contacted the acute pain team to discuss using Abstral in this way. The complainant confirmed with ProStrakan that it had no data to support this indication.

At this point the complainant became aware of the meeting. Since then he had had a meeting with the

representative and her line manager. They initially contested the complainant's view of the licence and whether their product was licensed but they also apologised. However the complainant considered that a more formal acknowledgement and possible rebuke of their activities might be in order.

When writing to ProStrakan, the Authority asked it to respond in relation to Clauses 2, 3.2, 15.2 and 15.9 of the Code.

RESPONSE

ProStrakan submitted that it appeared that the crux of this case rested on the use of Abstral in patients with urological cancers who underwent surgery. The complainant had raised concerns that use of the product in such circumstances was off-label, and as such the discussion of this use by a representative constituted off-label promotion. ProStrakan also noted that the complainant appeared not to have attended the meeting where the alleged discussion took place, but was made aware of the meeting afterwards as a consequence of an individual contacting the acute pain team.

While ProStrakan fully respected the complainant's concerns, it noted that the use of Abstral in the patient group described above was discussed in the meeting by ProStrakan's representative purely on the basis that patients with urological cancers might still be subject to breakthrough cancer pain post-operatively despite receiving other opioid treatment for chronic cancer pain. While radical surgery might be curative for some patients, not everyone with urological cancer would be suitable for radical procedures or subject to a curative outcome; surgery might instead focus on debulking tumours and/or relieving urological obstruction. In such cases the patient would still have cancer and thus potentially be subject to episodes of breakthrough cancer pain. In such cases the use of Abstral to relieve this pain would be appropriate and within licence.

ProStrakan's records showed that one of its representatives held a meeting in the urology department of the hospital but that this meeting was held in early May, not in late June as stated by the complainant. The meeting (held in early May) was a urology department event which was held regularly to meet with industry representatives. At this meeting a second representative presented on both Abstral and Tostran (testosterone) 2% Gel. The presentation on Abstral was run from an iPad (Abstral App, ref M017/0580c). A hard copy of the item was provided. As the meeting was part of an ongoing series organised by the urology department no formal agenda was produced and no additional materials were provided to the attendees. The meeting was attended by urologists and associated multidisciplinary health professionals.

When questioned about the meeting the representative mentioned that some of the urologists discussed the post-operative use of Abstral. They were interested in the use of the product and requested a follow-up call to the surgical recovery nurse that supported their team.

The representative stipulated that, to the best of her recollection, discussion centred around the post-operative use of Abstral in patients with urological cancers, specifically the urologists were interested in the possible use of Abstral for breakthrough pain in cancer patients post-operatively, eg the use of Abstral for episodes of breakthrough pain that occurred when cancer patients started to mobilise again following a surgical procedure. The representative considered that this use was within licence as the product would still be used to treat breakthrough cancer pain in patients with urological cancers.

ProStrakan submitted that the follow-up call to the surgical recovery nurse was made in late May. This visit was supervised by the representative's manager who was on a field visit with her that day. During this call the use of Abstral was discussed, but these discussions were strictly held within the licensed indication as evidenced by the field visit report which specifically mentioned that the promotion was within licence and that the nurse in question was clear about the licensed indication. Promotion of Abstral within its licensed indication was very important to ProStrakan and the risk management plan for Abstral, and as such was evaluated and assessed regularly on field visits. A second visit was made to this nurse in late June, but again discussions were regarding the licensed indication of Abstral.

On the Friday following this meeting the representative's manager was contacted by the complainant to discuss the use of Abstral in the hospital. As a consequence, a meeting was arranged in July between the second representative, the complainant and the first representative. ProStrakan submitted that during this meeting the three participants discussed the promotion of Abstral and its licensed indication. As ProStrakan understood it, the complainant's view of post-operative use differed slightly from ProStrakan's, as he put forward the view that cancer patients who had undergone surgery to remove the cancer were no longer cancer patients, and thus not appropriate patients for treatment with Abstral.

ProStrakan agreed with the complainant on this point. A patient who had been cured of cancer was no longer subject to breakthrough cancer pain, and was thus ineligible to be treated with Abstral. However, as detailed above, this was not what was promoted by the ProStrakan representative during the postgraduate meeting in early May. Not every patient undergoing surgery for urological cancer would be cured, and as such some might still suffer breakthrough cancer pain. Given that this was the case, ProStrakan considered that use of the product in these patients, and promotion of Abstral to the health professionals that treated them, was both appropriate and within the Code.

ProStrakan made every effort to ensure that the promotion of its products was conducted in a compliant and ethical manner. Not only was the initial training that its representatives received very important, but it also ensured that this training continued during their time with ProStrakan. Field

visits, in which a representative was observed in situ by his/her manager, were common. These ensured that high standards were maintained in all aspects of an individual's working life. During her time with ProStrakan the first representative had regularly received field visits from her line manager. These visits had consistently demonstrated that she had a clear and accurate understanding of the licensed indication for Abstral.

While ProStrakan respected the complainant's view it believed that the promotion of Abstral by its representatives had at all times been within the licensed indication, and thus a breach of Clause 3.2 was not warranted.

Further to this, ProStrakan had found no evidence that either of its representatives acted in contravention of this indication and argued that Clause 15.2 had not been breached.

A copy of the training material (Abstral Training Manual, ref M017/0456) used to clarify the licensed indication for Abstral was provided. ProStrakan submitted that the document to instruct its representatives on the way in which they should conduct themselves was sufficiently clear, and that it did not advocate a course of action that was likely to lead to a breach of the Code. There was no breach of Clause 15.9.

As a consequence ProStrakan also believed that a ruling of a breach of Clause 2 was not justified in this instance.

In response to a request for further information, ProStrakan stated that the meeting with the nurse in late June was not the meeting referred to by the complainant. However, without the ability to ask the complainant directly it was not possible to be certain.

ProStrakan agreed that a meeting was indeed scheduled with the urology department to discuss the use of Abstral. However, it believed that the complainant was mistaken about the date on which it occurred. ProStrakan's records showed that this meeting was held in early May. It was the only meeting held by the representative that fitted the complainant's description.

The meeting in late June was only attended by the representative, her manager and the nurse in question. No presentation was given. The meeting focused exclusively on the licensed indication as demonstrated by the field visit report. Field visit reports were provided for the meetings attended by the manager.

In response to a request for further information, ProStrakan noted that the meeting in the urology department in early May was attended by two urology consultants, two unnamed house officers and one other unnamed individual. The discussion was about the use and titration of Abstral (including its licensed indication) and patients that might be suitable for Abstral (including post-operative use in patients with cancer suffering from breakthrough cancer pain). ProStrakan provided details of which pages of the Abstral App were used by the representative in a presentation that lasted almost thirty minutes.

At the follow-up meeting in late May with the surgical recovery nurse no presentation was given and the discussion was about the use and titration of Abstral (stressing its licensed indication), end of life care, focusing on the treatment of breakthrough cancer pain and the potential advantages of Abstral to patients (specifically to those with renal impairment or who wished to be at home).

At a second meeting with the surgical recovery nurse in late June, again no presentation was given, and this time the discussion was on the use and titration of Abstral (including its licensed indication), quality of life for palliative care patients and the role that Abstral could play in improving quality of life for patients with breakthrough cancer pain.

ProStrakan noted that the complainant did not attend any of the meetings mentioned above, and thus was not present when the alleged off-licence discussion occurred.

ProStrakan reiterated that post-operative use of Abstral did not necessarily constitute off-label promotion. The representative in question stated that to the best of her recollection, discussion centred around the post-operative use of the product in patients with urological cancers, specifically stating that the urologists were interested in the possible use of Abstral for breakthrough pain in cancer patients post-operatively, eg the use of Abstral for episodes of breakthrough pain that occurred when cancer patients started to mobilise again following a surgical procedure. She stipulated that she considered that this use was within licence, as the product would still be used to treat breakthrough cancer pain in patients with urological cancers.

The presentation on Abstral was exclusively focused on use of the product within its licensed indication. According to the representative, participation in the discussion following the presentation had been limited, but that her understanding was that post-operative use in cancer patients suffering from breakthrough cancer pain was in licence.

PANEL RULING

The Panel noted that the complainant had not responded to the Panel's request for comments on the company's responses. It was often useful for the Panel to have comments on the response in cases like this where there appeared to be a difference of opinion. It was for the complainant to prove his/her complaint on the balance of probabilities. There appeared to be a difference of opinion as to when the meeting had taken place. The complainant referred to a meeting in late June and ProStrakan referred to a meeting in early May with the hospital urology department and follow up meetings with the surgical recovery nurse in late May and late June.

The Panel noted that the issue was in relation to using Abstral post-operatively following urological surgery. In the complainant's view this was outside the licence. ProStrakan submitted that its representative had discussed the use of Abstral in patients with urological cancers undergoing surgery purely on the basis that such patients might still be subject to breakthrough pain post-operatively despite receiving other opioid treatment for chronic cancer pain. Urological surgery might be focussed on debulking tumours and/or relieving urological obstruction. In such cases the patient would still be a cancer sufferer. ProStrakan agreed with the complainant that if surgery removed the cancer the patient would not have breakthrough cancer pain.

The Panel considered that it was important that representatives were very clear about the indications for use of the products they promoted. It would be unacceptable to promote Abstral in patients who did not have cancer however there was no evidence that this had happened. The Panel considered that the complainant had not proven his case on the balance of probabilities and no breach of Clause 3.2 was ruled. Consequently the Panel did not consider that the representative had failed to maintain a high standard of ethical conduct or failed to comply with the Code. No breach of Clause 15.2 was ruled.

The representative had presented from the Abstral App including an introduction to breakthrough cancer pain. The Panel noted that the presentation did not give the full indication. The brand logo referred to breakthrough cancer pain but there was no mention that patients needed to be using opioid therapy for chronic cancer pain. The Panel considered that this would have been helpful but the absence in the particular circumstances of this case did not amount to a breach of the Code.

The Panel did not consider that the briefing material advocated a course of action likely to breach the Code and thus no breach of Clause 15.9 was ruled.

Given its rulings above the Panel decided that there was no breach of Clause 2 and ruled accordingly.

Complaint received **16 July 2012**

Case completed **5 October 2012**

ANONYMOUS v SHIRE

Alleged promotion prior to the grant of a marketing authorization

An anonymous, non-contactable complainant who referred to him/herself as a health professional managing ADHD (attention deficit hyperactivity disorder) complained that an experienced MSL [medical science liaison] from Shire discussed with him/her an amphetamine medicine not licensed in the UK which Shire planned to launch next year [Vyvance (lisdexamphetamine mesylate) (LDX)]. The complainant alleged that Shire had instructed the MSLs to create 'noise' in the market about the new medicine and that they were set targets for the number of physicians willing to prescribe LDX or speak about it. The complainant further alleged that Shire also encouraged specialists to try the medicine on a 'named' scheme for patients.

One of the complainant's consultant colleagues often attended a two day monthly advisory panel meeting and recently attended another one. This was the third or fourth such Shire meeting this person had attended in 2012. The complainant had no doubt this busy consultant was likely to write many prescriptions for the new medicine.

The detailed response from Shire is given below.

The Panel noted that the complainant had provided little information and no documentation to support his/her complaint. As with any complaint, the complainant had the burden of proving his/her complaint on the balance of probabilities; the matter would be judged on the evidence provided by the parties.

The Panel noted Shire's submission that the MSL role was non-promotional and provided medical support for unsolicited enquiries about all of Shire's ADHD medicines. A document submitted by Shire entitled 'Clinical Development and Medical Affairs Guidance' described them as field counterparts to office-based medical affairs staff. They were not incentivized based on sales of medicines and targets were not set for interactions with health professionals.

The Panel noted from the job description submitted by Shire that a senior MSL reported to the associate director, international medical science liaison. The first 'essential function' noted on the job description was 'Through unsolicited requests for medical and scientific information, develop and raise Healthcare Professionals' level of understanding of medical and scientific data, using oral discussions, presentations and other appropriate media/techniques'. Other 'essential functions' included participation in cross-functional initiatives, delivery of medical education presentations and information gathering. One of the key skills and competencies listed referred to '…the non-promotional activities of this role'.

The 'Clinical Development and Medical Affairs Guidance' document stated that the medical and scientific activities of MSLs were proactive and reactive. The proactive activities included, *inter alia*, key opinion leader introductions and on-going relationship management, research support, issue management, disease state discussions and collection and input into scientific platforms. The reactive activities included, *inter alia*, responding to unsolicited requests for information and presentation on topics such as formulary/health economic outcomes resource, disease state and/or scientific data. Section VI of this document, 'Interactions with HCPs' [health professionals] noted that MSLs might meet health professionals to, *inter alia*, respond to unsolicited requests for information and to provide 'in-depth on-label information about Shire product, including changes to approved label'. The Panel considered that it was not clear as to whether this latter activity was proactive or reactive.

The Panel noted that a number of briefing documents for medical affairs were provided in relation to Vyvanse. A fact sheet contained a number of questions about the availability of LDX, mechanism of action, key data and side effects. The document was marked 'Reactive Use Only' and noted that the medicine was not yet licensed in the UK.

Two presentations, described by Shire as medical affairs training slides to respond to unsolicited medical information requests from health professionals, detailed results of two LDX studies in children and adolescents. The Panel noted that there appeared to be no briefing documents for Shire employees about the use of these presentations and there was no statement on any of the slides that the presentations were only to be used reactively.

The Panel noted that a further question and answer document entitled 'Availability of Shire ADHD products May 21, 2012' was marked 'For Internal Use Only. Not to be Forwarded or Distributed', but there was no indication that the information was only to be used reactively. In response to a question on which countries, *inter alia*, LDX was approved and marketed, this document stated that Vyvanse was approved and marketed in the US and Canada and was recently launched in Brazil under the name of Venvanse. A further question was 'Is Vyvanse [LDX] available via a 3rd party importer outside of the US?' and the answer stated was 'Shire only markets and promotes its products in accordance with regulatory guidelines in the countries where they are approved'. The document then stated that, if pressed, details could be provided of a specialist company which imported medicines on a named patient basis.

The Panel noted that the parties' accounts differed. A decision had to be made on the evidence before it. The complainant had provided no evidence in relation to his/her allegation that MSLs had been instructed to create 'noise' in the market about LDX, that they were set targets in relation to contacts with health professionals or that they encouraged health professionals to try LDX on a named patient basis. The Panel had some concerns about the material; it was not clear whether the MSL role was entirely reactive when it came to on-label discussion of Shire products and some of the briefing material about LDX could have been clearer that information on the medicine should only be provided in response to an unsolicited request. The Panel was also concerned about the absence of briefing materials indicated above. However, the Panel considered that there was no evidence to suggest that the MSLs had promoted, or had been briefed to promote, LDX before a marketing authorization that permitted its sale or supply was granted, nor was there evidence that the MSLs had promoted the use of LDX via a named patient programme. No breaches of the Code were ruled.

Turning to Shire's advisory boards, the Panel noted that advisory boards were a legitimate activity; all of the arrangements had to comply with the Code. The company must be able to demonstrate that it had a bona fide need for the advice being sought. 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 meaningfully contribute to the purpose and expected outcomes of the meeting. The number of participants should be limited so as to allow active participation by all. The agenda should allow adequate time for discussion. The overall number of meetings should be limited and both the number of meetings and the number of participants at each should be driven by need and not the invitees' willingness to attend. Invitations to participate in an advisory board meeting should state the purpose of the meeting, the expected advisory role and the amount of work to be undertaken.

The Panel noted that Shire's global policy on advisory boards stated that advisory boards must be solely intended and necessary to fulfill a legitimate, unmet business need for information, advice and feedback from participants regarding Shire products or other topics relevant to Shire business and must be designed to elicit bona fide information from advisors. The advisory board should address questions in order to provide advice or feedback that had not previously been provided by either the advisors or through market research or otherwise.

The Panel noted that the complainant had not identified the individual who he/she alleged had attended a number of Shire's advisory boards. The Panel noted that it was not necessarily unacceptable for an individual to attend more than one such advisory board so long as the meetings themselves and the associated arrangements, including the selection of candidates, complied with the Code. In addition the complainant had referred to the subsequent likelihood of this individual writing many prescriptions for the new product. The Panel's view was that it thus had to consider whether the overall arrangements for the advisory boards were promotional. The Panel further noted that the complainant had the burden of proving his/her complaint on the balance of probabilities. Given that the complainant was non-contactable, the Panel could not ask further questions in relation to the identity of his/her colleague, establish that that person had attended a number of advisory boards or consider the legitimacy of that colleague attending those advisory boards in relation to LDX.

The Panel noted that since January 2011 Shire had run ten advisory boards in the UK related to ADHD: an inaugural market access advisory board in January 2011; three clinical advisory boards (October 2011 Clinicians advisory board, January 2012 ADHD clinicians adolescent advisory board, June 2012 LDX advisory board on safety data and post-marketing surveillance data); two on economic/budget modelling (January 2011 and June 2012); a pharmacy advisory board (March 2012 which looked at *inter alia* information to budget holders) and three miscellaneous advisory boards (April 2012 Working group meeting, LDX UK market access advisory board, June 2012 Treatment individualization advisory board and February 2012 2nd International ADHD advisory board).

The Panel further noted Shire's submission that the marketing authorization approval for LDX was expected in the first quarter of 2013 and the application was currently under review by the Medicines and Healthcare products Regulatory Agency (MHRA).

The Panel noted the agendas and presentations provided by Shire. When determining whether there was a legitimate unmet question which Shire needed to address the Panel noted Shire's long standing commercial interest in the therapy area and thus considered that it would be reasonably familiar with the ADHD market. Nonetheless, LDX would be the first long-acting pro-drug of d-amphetamine and changes to the NHS meant that ADHD service provision might change. The Panel thus considered that there would be legitimate questions which the company needed to address before the launch of LDX.

The Panel noted the agenda items presented and/or discussed at each advisory board and was concerned about the number of meetings and the overlap between the agendas. Some topics or closely similar topics were discussed at more than one advisory board.

The Panel noted some of its concerns outlined above in relation to the number of advisory boards held on very similar topics over a relatively short period of time. It also noted that the complainant was anonymous and non-contactable and that the Panel could not ask him/her for further details about the health professional in question. The Panel considered that the complainant had not established

that the selection and attendance of the unidentified health professional at several advisory board meetings was contrary to the requirements of the Code. The complainant had not established that the advisory boards had promoted LDX before the grant of a marketing authorization that permitted its sale or supply. On the very narrow grounds of the allegation, no breaches of the Code were ruled.

An anonymous, non-contactable complainant who referred to him/herself as a health professional managing ADHD (attention deficit hyperactivity disorder) complained about the activities of Shire Pharmaceuticals Limited. Shire marketed Equasym XL (methylphenidate extended release) for the management of ADHD and planned to launch Vyvance (lisdexamphetamine mesylate (LDX)) in 2013.

COMPLAINT

The complainant stated that he/she was approached by an experienced MSL [medical science liaison] from Shire to discuss an amphetamine medicine not licensed in the UK which Shire planned to launch next year. The MSLs were allegedly under clear instructions from the company to create 'noise' in the market about the new amphetamine based medicine. The MSLs were set targets to achieve every quarter and these included the number of physicians who were willing and ready to write prescriptions for the new medicine which was not licensed and the number of specialists happy to speak about the new medicine and these figures were monitored every couple of months or so. The complainant further alleged that Shire also encouraged specialists to try the medicine on a 'named' scheme for patients where patients had to pay high costs privately. This intense campaign had created a perception of inadequacy and dissatisfaction with the current widely prescribed and very effective products available in the NHS such as long-acting methylphenidate which risked an unfair drain on already squeezed resources in favour of an unlicensed medicine in the UK.

The complainant noted that sales representatives always declined to discuss unlicensed medicines and cited ABPI rules. The complainant queried whether MSLs were bound by the ABPI. This was confusing.

One of the complainant's consultant colleagues often attended a two day monthly advisory panel meeting and recently attended another one. This was the third or fourth such Shire meeting this person had attended in 2012. The complainant had no doubt this busy consultant was likely to write many prescriptions for the new medicine. The complainant stated that the Medicines and Healthcare products Regulatory Agency (MHRA) and the media stated that companies could not promote unlicensed medicines and that such activities were unlawful and sometimes harmed patients.

When writing to Shire, the Authority asked it to respond in relation to the requirements of Clauses 3.1, 9.1 and 2 of the 2012 Code.

RESPONSE

Shire refuted the alleged breaches of Clauses 3.1, 9.1 and 2 of the Code and stated that the complainant's allegations were vague and no proof was provided, and as the complainant was anonymous further specific details could not be confirmed. Following an investigation into the conduct of all of Shire MSLs working in the therapeutic area, Shire was satisfied that they worked within its policies and the Code.

In their contact with health professionals Shire's MSLs must act only in accordance with their defined roles and responsibilities. Furthermore, the MSLs had not been instructed to create 'noise' in the market about any product, they did not have targets based on physician visits and they did not encourage physicians to try any products on a named patient scheme. The complainant had also referred to advisory boards held in relation to the therapeutic area and to Vyvanse. As set out below, all of Shire's advisory boards had been held in accordance with Shire's relevant standard operating procedures (SOPs) which were consistent with the Code.

Shire submitted that it had not found any evidence to support the allegations. Shire had not conducted pre-licence promotion and would never allow such promotion by any of its staff. It was confident that there had been no breach of the Code.

Shire submitted that it had two MSLs who supported the UK ADHD therapy area. Shire's MSLs carried out non-promotional functions and reported to the medical affairs department. They provided medical support for unsolicited medical enquiries in relation to all of Shire's ADHD products. MSLs were not incentivized on product sales and no targets were set for the number of MSL interactions with health professionals. Shire submitted that its MSLs performed a strictly non-promotional role and therefore they did not promote the prescription, supply, sale or administration of any medicine.

The MSL teams had been clearly briefed and trained in this role with clear and defined responsibilities. A copy of the MSL job description was provided.

The role and objectives of Shire's MSLs was set out in the Clinical Development and Medical Affairs document: Medical Science Liaison activities, which stated that:

> 'MSLs act as field counterparts to office-based Shire Medical Affairs staff. The primary role of the MSL is to address the scientific needs of HCPs [healthcare professionals] by fostering fair and balanced scientific communications that are not misleading. To further ensure that Shire MSLs conduct appropriate medical and scientific communications, the activities of the Shire MSLs are divided into two categories: proactive and reactive.'

The document went on to list various proactive activities which included, *inter alia*, interactions with key opinion leaders (KOLs); research support; issue

management and disease state discussions. The reactive activities listed included responding to unsolicited requests for information from HCPs and others; research support; delivery of presentations; attendance at advisory boards; publication support and issues follow-up.

The document went on to detail the appropriate interactions of MSLs with sales and marketing. It was clearly stated that MSLs and sales representatives had different roles and should work independently of each other and that joint sales calls and/or in-person meetings involving sales representatives and MSLs were not permitted except where a sales representative was introducing the MSL to a health professional at an initial meeting following that health professional's unsolicited request for detailed scientific or medical information. In this circumstance, the different roles of the MSL and sales representative should be explained to the health professional, and the sales representative should not participate during the scientific discussions between the MSL and health professional.

Shire provided copies of materials used by its MSLs in relation to responding to unsolicited medical information requests.

The MSLs did not meet the definition of 'representative' as defined in Clause 1.6 of the Code:

> 'The term "representative" means a representative calling on members of the health professions and administrative staff in relation to the promotion of medicines.'

Shire submitted that its MSLs did not initiate 'calls'. In the UK, since January 2012, the two MSLs working in ADHD had 131 scientific exchange interactions with health professionals (primarily responding to unsolicited medical enquiries on any Shire products especially Equasym XL, key opinion leader introductions, disease state discussions and research support), which included MSL attendance at Shire advisory boards.

Shire stated that all MSL interactions with health professionals related to any Shire product must be unsolicited and in response to specific requests. These 131 interactions included four LDX-related one-to-one medical information interactions with health professionals, each of which was in response to an unsolicited request for information.

MSLs only attended advisory boards as ADHD experts when requested to do so by the medical affairs department. An MSL was present at seven of the advisory boards.

Shire submitted that MSLs' performance was measured against the core responsibilities contained within the Clinical Development and Medical Affairs document: Medical Science Liaison activities. Specific objectives for MSLs were to provide accurate and timely responses to medical enquiries, facilitate scientific exchange, provide research support on request from Shire R&D and to comply with Shire's policies and the Code.

Marketing authorization approval for LDX was anticipated in the first quarter of 2013. The application was currently under review by the MHRA which was the reference member state under the decentralized procedure.

Shire stated that all MSL product-related interactions or scientific discussions with health professionals were unsolicited, reactive and in response to specific requests. This applied to any approved Shire products, including Equasym XL and pre-approval or pipeline products. The guidelines for MSLs in relation to discussion of products was set out in the MSL activities documents. Whenever information was provided to health professionals, MSLs ensured that the information was medical and/or scientific in nature, and that it was not provided in a promotional manner. Sales force promotional materials were never used or distributed by MSLs.

In response to specific questions posed by a health professional, the MSL, depending upon the question, might provide information about a Shire product that was: 'on-label' (ie consistent with the product's approved label); 'off-label' (only if in response to an unsolicited request); or related to a pre-approval or 'pipeline' product.

- If the health professional requested 'off-label' information, the MSL must communicate that the information provided might not be consistent with the approved product labeling.
- Responses to unsolicited requests for information must be narrowly tailored to the question and not be seen as an opportunity to discuss other topics.
- Where pipeline products were concerned, responses must not represent that an investigational new medicine was safe or effective for the purposes for which it was under investigation. MSLs would use caution to avoid the perception of promotional activity by providing all available information regarding the pipeline product, with full disclosure of both positive and negative information.

MSLs might provide specific scientific information about competitor products which was in the public domain, if requested by the health professional. Also:

- MSLs must not discuss any off-label use of a non-Shire product; and
- MSLs must direct the health professional to the relevant pharmaceutical manufacturer.

Shire did not actively encourage nor did it promote named patient supply of LDX. However, the medicine was available through a third party importer in all countries where it did not have a marketing authorization, and where permitted under local laws.
MSLs could not proactively discuss LDX. The Medical Q&A on ADHD Product Availability set out how MSLs should answer specific questions about product availability:

> 'Q. Is Vyvanse available via a 3rd party importer outside the US?

Shire only markets and promotes its products in accordance with regulatory guidelines in the countries where they are approved.

If pressed: [Name of importer], a specialist company based in the UK, imports medicines on a 'named-patient' basis'* For specific information regarding this program or product availability, please contact [importer] directly. Contact details for [importer] are: [contact details were provided]

*Named-Patient refers to the supply of Products which do not have a product licence in the country of destination and/or which are not commercially available and are supplied to meet the special needs of a specific patient or patients under the order of a medical practitioner and in compliance with exceptions to the product licensing requirements in such countries.'

The further information on the import company could only be provided if the enquiring health professional insisted on information, which was the meaning of the instruction 'if pressed'.

Shire did not know how many patients received named patient supply or whether those patients had participated in an LDX clinical trial. The named patient supply scheme was entirely managed by the import company.

ADHD was a serious medical condition which presented as a complex and difficult to manage set of behaviours, often associated with poor provision of services and significant delay in care. Diagnosis most commonly occurred in primary school. As such the need to understand the NHS perspective, and the perspective of academic and practising clinicians, was key to the introduction of a new chemical entity in ADHD treatment.

Shire took responsibility within ADHD very seriously and had the challenge of gaining information about the care of children in the UK from several different constituents, some of whom had a wider range of healthcare responsibilities.

In order to meet the demands of this complex area Shire UK had held advisory boards to gather advice from or about: NHS management; academic clinicians; hospital clinicians and ADHD treatment (non LDX). Two international advisory boards had also been held in the UK. The agendas, invitations and attendance lists for all the meetings were provided.

The Shire advisory boards were conducted in accordance with the SOP which specifically applied ABPI standards to advisory boards held in the UK.

In summary, Shire submitted that one of its key priorities was to act with integrity and maintain the highest ethical standards. Its compliance procedures were central to this effort. A dedicated international team of specialists at Shire supported the UK team, including signatories, in maintaining compliance. Furthermore, Shire's MSLs were managed by a dedicated R&D management team and subjected to training and oversight by Shire's R&D compliance function.

Shire had not conducted pre-licence promotion and would never allow such promotion by any of its staff. LDX was widely prescribed in the US and was also marketed in Brazil and Canada. Child and adolescent psychiatrists were likely to know about this medicine from international colleagues, publications and the Internet.

Following a request for further information, Shire submitted that meeting reports for all advisory boards demonstrated that the intended objectives for each were achieved. Shire noted that the meeting reports for the international advisory boards had been reviewed, UK reports were not for dissemination and therefore did not require approval.

Shire submitted that ADHD was a complex disease area and there were many scientific and clinical topics upon which it needed to obtain expert advice. The advisory board meetings referred to were built around different topics in the management of ADHD that Shire must better understand in order to focus its planning and investment. These objectives had informed the selection of advisers for each meeting. Advisers were individually selected for each meeting based on their speciality, expertise and areas of special interest where those were directly relevant to the specific advice to be sought at the meeting.

Shire submitted that its medical affairs department selected advisers at the following advisory boards:

- October 2011, LDX Child Advisory Board (n=12)
- January 2012, LDX Adolescent Advisory Board (n=16)
- April 2012, LDX Working Group (product profile) (n=9)
- June 2012, LDX Advisory board - Safety data & post-marketing surveillance data (n=14)
- June 2012, Treatment Individualisation Advisory Board (n=12)

Shire's UK market access group selected advisers for the following advisory boards:

- January 2011, LDX UK Market Access Advisory Board (n=14)
- June 2012, Budget Impact Model advisory board (n=10)
- March 2012, Advanced Budget Notification Advisory Board (n=8)

Shire's health economics and outcomes research group selected the 6 advisers who attended the LDX economic modelling advisory board held in January 2011.

Twelve delegates attended each of the international advisory boards held in December 2011 and June 2012.

Shire's international medical affairs team selected advisers at the LDX abuse liability advisory board held in February 2012.

Shire submitted that more specific criteria for adviser selection included:

1 Speciality/areas of academic and/or clinical special interest;
2 Advisers' job roles and responsibilities, including patient sub-groups managed (such as children, adolescents, patients with ADHD and co-morbidities, patients within the criminal justice system). This was important information to Shire because ADHD patient sub-groups were managed and treated differently, for example children were often managed differently to adolescents or adults;
3 Prescribers and non-prescribers because ADHD was not always treated with pharmacological products. Non-pharmacological interventions were also an integral part of ADHD management pathways, as per the National Institute for Health and Clinical Excellence (NICE) guidelines/EU guidelines; and
4 Budget holders across all therapy areas and also those with specific ADHD responsibility to understand the interaction between the two and how the priorities are assessed.

Shire provided a breakdown of the subsistence, accommodation and other costs incurred at each meeting and slides sets for all presentations. Materials were not provided to delegates before, during or after the meetings. The meeting reports were prepared for 'Shire internal use only' and were not sent to the delegates. These reports were then referred to by relevant Shire colleagues as they planned their strategies and approaches in all areas of Shire's business going forward.

Shire submitted that, in relation to the January 2011 advisory board, it telephoned proposed advisers to seek their agreement in principal to participate and to ask them to save the date. Confirmation invitations were sent as a follow up (copies provided). The advisers were selected on the basis of their knowledge of ADHD services and policies in the UK and to satisfy the main objectives of the advisory board which were to understand the current service provision in the UK with respect to adolescent ADHD service users including the transition from child to adolescent and into adulthood.

The meeting in January 2011 was a market access advisory board and therefore the attendees were different from the advisory boards focused on the needs of prescribers. The introductions section of the meeting report (copy provided) described the main objectives of the meeting. As well as having commissioners, payers and health professionals present to answer Shire's questions about changes to the NHS, there was a representative from an ADHD patients group, a teacher, nurses, a special educational needs co-ordinator (SENCO) and also a consultant with expertise in substance misuse. These participants could provide valuable information on service provision. Attitudes to ADHD were very challenging in the UK so this meeting helped Shire to 'set the scene' and understand what the current issue were. ADHD care was multidisciplinary and teachers, SENCOs and nurses were often key members of community and mental health services (CAMHS) teams. This was very different from the treatment pathways for many other medical conditions when assessment, treatment and monitoring was restricted to a much more narrowly defined group of health professions. Shire hoped that it was apparent from the meeting report how useful this meeting was and how much was learnt from it.

Shire submitted that honoraria levels for all of its advisory boards were determined with reference to the adviser's specialty and level of expertise (including academic and clinical expertise) in order to provide fair market value compensation. Honoraria levels for each advisor were provided.

Shire noted that it engaged an independent healthcare consultant to provide certain services in relation to this meeting including preparation of slides, support on agenda development, attendance at the review meeting in January as well as facilitating and chairing the advisory board.

Shire confirmed that during the two day October 2011 meeting, dinner was provided at a restaurant close to the Royal College of Physicians and the hotel. The hotel was modest and not deluxe or lavish. A private dining room (set house menu) was used because it was anticipated that the participants might discuss proceeding of the advisory board over dinner. The subsistence offered was appropriate and not out of proportion to the occasion. In accordance with the Code, the costs involved did not exceed the level which the recipients would normally apply when paying for themselves.

No participant attended on the first day only. One participant attended on the second day of the meeting only and so was paid a reduced fee to reflect the level of her participation.

Shire confirmed that one of the attendees at the meeting in April and June 2012 was an independent and supplementary nurse who was an expert on the management of ADHD in the prison environment and a leading UK authority on misuse, abuse and diversion of abusable substances in youth offending. That delegate also had a specialist interest in addictions, prison work and forensic psychiatry and managed ADHD patients in this setting.

Shire submitted that it only provided overnight accommodation for advisory boards where necessary based on the length of the meeting or the adviser's individual circumstances. Relevant factors included the distance the adviser needed to travel and whether he/she was required for a pre-meeting briefing the night before. Hospitality was strictly limited to the purpose of the event. The level of subsistence offered was appropriate and not out of proportion to the occasion. In accordance with the Code, the costs involved did not exceed the level which the recipients would normally apply when paying for themselves.

Shire submitted details of participants who were provided with dinner and accommodation for the two day advisory board meeting in January 2012. The dinner provided an opportunity for the majority of the group to continue to discuss some of the key topics during the evening. No participant attended on the first day only, but one participant attended on the second day only. A reduced honorarium for one day's participation was paid.

Shire provided a copy of the final agenda for the advisory board in April and noted that one participant did not arrive until the second day and thus only received a reduced honorarium.

Shire provided a copy of the objectives statement referred to in the invitation for the budget impact advisory board in June 2012 and confirmed that only one participant received overnight accommodation.

Shire submitted that for another two advisory boards in June 2012, verbal invitations were extended by the MSLs and followed by a formal letter of engagement (copy provided). Accommodation was only offered to those with long and difficult journeys as the two meetings started at 8.30am and 9.30 am, respectively. No dinner was provided, only accommodation. Some delegates with long distance journeys declined the invitation for accommodation. Details of those who had overnight accommodation the nights before the meetings were provided.

Shire confirmed that the international advisory board in February 2012 was the second in a series of three meetings. The first was held in December 2011 in Zurich and the third was held in June 2012 in Paris. Copies of meeting agendas, invitations, delegate information and meeting reports were provided.

Shire confirmed that there were currently no other advisory boards planned.

Shire provided details of all Shire staff attendance at each advisory board. There were no specific briefing documents for these employees. However Shire staff who were involved with the advisory boards attended an initial planning meeting and subsequent meetings and/or teleconferences to ensure all staff were informed and updated on the objectives and content of the meeting, including their roles and responsibilities at the meetings. All Shire and agency participants were fully trained and aware of their ABPI responsibilities and the requirements of the Code.

Shire confirmed that there was a UK SOP for advisory boards (copy provided) and that it was currently finalising a new international SOP for which a new UK document would be in place.

Shire submitted that the advice it gathered from external experts in advisory boards was crucial to assist it in planning its investment and activities. Shire's advisers were selected individually based on their relevant knowledge and expertise.

Shire hoped that it had demonstrated that its UK ADHD advisory boards complied with the Code, did not constitute pre-market promotion and that it had maintained high standards and was therefore not in breach of Clauses 3.1, 9.1 or 2.

Shire hoped that LDX would be granted a licence in the UK because current ADHD therapy options were limited and a new therapy choice would help many patients and their families and provide value for the NHS.

Shire stated that ADHD care presented special challenges, especially in the UK where belief in ADHD as a medical condition was often disputed and access to services was delayed. At the heart of this issue were children of six years of age being considered for treatment with amphetamine. Shire therefore took this situation very seriously. Shire's efforts to understand those challenges and plan its activities accordingly was part of its philosophy which was 'to be as brave as the people we help' and 'to enable people with life altering conditions to lead better lives'.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable and had provided little information and no documentation to support his/her complaint. As with any complaint, the complainant had the burden of proving his/her complaint on the balance of probabilities; the matter would be judged on the evidence provided by the parties.

The Panel noted Shire's submission that the MSL role was non-promotional and provided medical support for unsolicited enquiries in relation to all of Shire's ADHD medicines. A document submitted by Shire entitled 'Clinical Development and Medical Affairs Guidance' described them as field counterparts to office-based medical affairs staff. They were not incentivized based on sales of medicines and targets were not set for interactions with health professionals.

The Panel noted from the job description submitted by Shire that a senior MSL reported to the associate director, international medical science liaison. The first 'essential function' noted on the job description was 'Through unsolicited requests for medical and scientific information, develop and raise Healthcare Professionals' level of understanding of medical and scientific data, using oral discussions, presentations and other appropriate media/techniques'. This accounted for 45% of the role's function. Other 'essential functions' were to participate in the company's cross-functional initiatives; deliver quality medical education presentations and gather information. One of the key skills and competencies listed was 'Deep understanding and knowledge of local regulations and codes of practice for the pharmaceutical industry, in particular as they apply to the non-promotional activities of this role'.

The 'Clinical Development and Medical Affairs Guidance' document stated in Section II, Overview of Roles and Responsibilities of Shire MSLs, that the medical and scientific activities of MSLs were divided into two categories; proactive and reactive. The reactive activities included, *inter alia*, key opinion leader introductions and on-going relationship management, research support, issue management, disease state discussions and collection and input into scientific platforms. The reactive activities included, *inter alia*, responding to unsolicited requests for information and presentation on topics such as formulary/health economic outcomes resource, disease state and/or scientific data. Section VI of this document, Interactions with HCPs [health professionals] noted that MSLs might meet health professionals to, *inter alia*, respond to unsolicited requests for information and to provide 'in-depth on-label information about Shire product, including changes to approved label'. The Panel considered that the latter was not clear as to whether this activity was proactive or reactive, but the impression created by separating this activity from responding to unsolicited requests was that discussion of on-label information was proactive. This appeared to be inconsistent with the statements in Section II of the document and with the MSL job description. Such proactive activity might also satisfy the definition of a representative in Clause 1.6.

The Panel noted that a number of briefing documents for medical affairs were provided in relation to LDX. A fact sheet (UK/LO/COPR/11/0172) contained a number of questions about the availability of LDX, mechanism of action, key data and side effects. The document was marked 'Reactive Use Only' and noted that the medicine was not yet licensed in the UK. However, the document also stated that it was for UK health media and the Panel questioned whether this was in fact a document intended to be used by Shire communications personnel rather than MSLs.

A presentation, described by Shire as a medical affairs training slide deck to respond to unsolicited medical information requests from health professionals detailed results of a European safety and efficacy study of LDX in children and adolescents (SPD489-325). The Panel noted that there appeared to be no briefing document for Shire employees about the use of this presentation and there was no statement on any of the slides that the presentation was only to be used reactively. A further presentation, SPD489-326 Summary of Results, was similarly described by Shire and detailed the results of a Phase III safety and efficacy trial of LDX in children and adolescents aged 6-17 with ADHD. Again, there did not appear to be any briefing document for this presentation or indication on the slides that they should only be used reactively. A statement on the title slide read 'Confidential Material Not For Distribution'. Two separate question and answer documents for these trials (SPD486-325 and SPD489-326) were provided and both were entitled 'Medical Q&A for reactive statements'.

The Panel noted that a further question and answer document entitled 'Availability of Shire ADHD products May 21, 2012' was marked 'For Internal Use Only. Not to be Forwarded or Distributed', but there was no indication that the information was only to be used reactively. In response to a question on which countries, *inter alia*, LDX was approved and marketed, this document stated that Vyvanse [LDX] was approved and marketed in the US and Canada and was recently launched in Brazil under the name of Venvanse. A further question was 'Is Vyvanse [LDX] available via a 3rd party importer outside of the US?' and the answer stated was 'Shire only markets and promotes its products in accordance with regulatory guidelines in the countries where they are approved'. The document then stated that, if pressed, details could be provided of a specialist company which imported medicines on a named patient basis.

The Panel noted that the parties' accounts differed. A decision had to be made on the evidence before it. The complainant had provided no evidence in relation to his/her allegation that MSLs were under clear instruction to create 'noise' in the market about LDX, that they were set targets in relation to contacts with health professionals or that they encouraged health professionals to try LDX on a named patient basis. The Panel had some concerns about the material; it was not clear whether the MSL role was entirely reactive when it came to on-label discussion of Shire products and some of the briefing material about LDX could have been clearer that information on the medicine should only be provided in response to an unsolicited request. The Panel was also concerned about the absence of briefing materials indicated above. However, the Panel considered that there was no evidence to suggest that the MSLs had promoted, or had been briefed to promote, LDX before the granting of a marketing authorization that permitted its sale or supply, nor was there evidence that the MSLs had promoted the use of LDX via a named patient programme. No breach of Clause 3.1 was ruled. Subsequently no breaches of Clauses 9.1 and 2 were ruled.

Turning to Shire's advisory boards, the Panel noted that advisory boards were a legitimate activity; all of the arrangements had to comply with the Code. The company must be able to demonstrate that it had a bona fide need for the advice being sought. 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 meaningfully contribute to the purpose and expected outcomes of the meeting. The number of participants should be limited so as to allow active participation by all. The agenda should allow adequate time for discussion. The overall number of meetings should be limited and both the number of meetings and the number of participants at each should be driven by need and not the invitees' willingness to attend. Invitations to participate in an advisory board meeting should state the purpose of the meeting, the expected advisory role and the amount of work to be undertaken.

The Panel noted that Shire's global policy on advisory boards (06-227Global HGT/ExUSROWSP) stated that advisory boards must be solely intended and necessary to fulfill a legitimate, unmet business need for information, advice and feedback from participants regarding Shire products or other topics relevant to Shire business and must be designed to elicit bona fide information from advisors. The advisory board should address questions in order to provide advice or feedback that had not previously been provided by either the advisors or through market research or otherwise, unless there was a valid, fact-based reason to conclude that i) the advice or feedback would not duplicate the answers, and/or ii) circumstances had changed such that additional advice or feedback was needed, or it was reasonable and necessary to determine if the previous advice was still valid.

The Panel noted that the complainant had not identified the individual who he/she alleged had attended a number of Shire's advisory boards. The Panel noted that it was not necessarily unacceptable for an individual to attend more than one such advisory board so long as the meetings themselves and the associated arrangements including the selection of candidates complied with the Code. In addition the complainant had referred to the subsequent likelihood of this individual writing many prescriptions for the new product. The Panel's view was that it thus had to consider whether the overall arrangements for the advisory boards were promotional. The Panel further noted that the complainant had the burden of proving his/her complaint on the balance of probabilities. Given that the complainant was non-contactable, the Panel could not ask further questions in relation to the identity of his/her colleague, establish that that person had attended a number of advisory boards or consider the legitimacy of that colleague attending those advisory boards in relation to LDX.

The Panel noted that since January 2011 Shire had run ten advisory boards in the UK related to ADHD: an inaugural market access advisory board in January 2011; three clinical advisory boards (October 2011 Clinicians advisory board, January 2012 ADHD clinicians adolescent advisory board, June 2012 LDX advisory board on safety data and post-marketing surveillance data); two on economic/budget modelling (January 2011 and June 2012); a pharmacy advisory board (March 2012 which looked at *inter alia* information to budget holders) and three miscellaneous advisory boards (April 2012 Working group meeting, LDX UK market access advisory board, June 2012 Treatment individualization advisory board and February 2012 2nd International ADHD advisory board).

The Panel further noted Shire's submission that the marketing authorization approval for LDX was expected in the first quarter of 2013 and the application was currently under review by the MHRA which was the reference member state under the decentralized procedure.

The Panel noted the agenda and presentations provided by Shire. When determining whether there was a legitimate unmet question which Shire needed to address the Panel noted Shire's long standing commercial interest in this therapeutic market and thus considered that it would be reasonably familiar with the ADHD market. Nonetheless, LDX would be the first long-acting pro-drug of d-amphetamine and changes to the NHS meant that ADHD service provision might change. The Panel thus considered that there would be legitimate questions which the company needed to address before the launch of LDX.

The Panel noted the agenda items presented and/or discussed at each advisory board. The Panel had some concerns about the number of meetings and the overlap between the agendas. Some topics or closely similar topics were discussed at more than one advisory board, eg current treatments for ADHD appeared to have been discussed at the meetings with clinicians in October 2011, January 2012 and April; service provision in ADHD was discussed at the meetings in January 2011, October 2011 and January 2012; the ADHD landscape (October, April and whilst not on the agenda it was listed as the first objective in the meeting report for the meeting held in January); current prescribing environment in primary and secondary care (March and June). The slides presented by Shire on these topics demonstrated an in-depth knowledge of the subject matter. One slide included the claim 'Shire's expertise and leadership in ADHD established'.

The Panel noted some of its concerns outlined above in relation to the number of advisory boards held on very similar topics over a relatively short period of time. It also noted its comments above that, as the complainant was non-contactable, the Panel could not ask him/her for further details about the health professional in question. The Panel considered that the complainant had not established that the selection and attendance of the unidentified health professional at several advisory board meetings was contrary to the requirements of the Code. The complainant had not established that the advisory boards had promoted LDX before the grant of a marketing authorization that permitted its sale or supply. On the very narrow grounds of the allegation, no breach of Clause 3.1 was ruled. The Panel subsequently ruled no breach of Clauses 9.1 and 2.

Complaint received **6 August 2012**

Case completed **15 October 2012**

CASE AUTH/2529/9/12

ANONYMOUS/DIRECTOR v VIFOR

Breach of undertaking

An anonymous GP complained about advertisements issued by Vifor global which had been the subject of a voluntary admission by Vifor Pharma, Case AUTH/2473/1/12.

In Case AUTH/2473/1/12, Vifor voluntarily admitted that advertisements had not been certified prior to publication and the Panel ruled a breach of the Code. During its consideration of the case, however, the Panel further noted that, as acknowledged by Vifor in subsequent correspondence, the advertisements featured the strapline 'Mastering the art of iron therapy' which had been ruled in breach in Case AUTH/2423/7/11. However, as Vifor's initial voluntary admission only related to a lack of certification, the Panel could make no ruling with regard to the possible breach of undertaking. Given the importance of complying with undertakings, Vifor was informed of the position and the matter was noted in the case report. Having read that case report, the complainant now asked for the breach of undertaking to be investigated.

As the complaint concerned an alleged breach of undertaking it was taken up by the Authority in the name of the Director as the Authority was responsible for ensuring compliance with undertakings.

The detailed response from Vifor is given below.

The Panel noted that in its consideration of Case AUTH/2473/1/12 it had been extremely concerned to note that the advertisements at issue featured the strapline 'Mastering the art of iron therapy' which was ruled in breach in Case AUTH/2423/7/11. Vifor had accepted the ruling in that case and provided the relevant undertaking and assurance. The advertisements with the same strapline were therefore potentially in breach of that undertaking. The Panel noted that in Case AUTH/2473/1/12 Vifor had voluntarily brought to the Authority's attention advertisements containing the same strapline but had only admitted a breach of the Code with regard to lack of certification. The Constitution and Procedure did not allow the Panel to consider matters which were not subject of a complaint or a voluntary admission and nor was there any mechanism under which it could instigate a fresh complaint. The Panel could only point the matter out to the company concerned and note it in the case report. The Panel's comments in this regard appeared to have prompted the complaint now at issue. It was very unusual to receive a subsequent complaint about such a matter.

The Panel considered that the repeated use of the claim 'Mastering the art of iron therapy' breached the undertaking given in Case AUTH/2423/7/11 and in that regard high standards had not been maintained. Breaches of the Code were ruled.

The Panel noted the importance of undertakings and considered that failure to comply with the undertaking and assurance previously given in Case AUTH/2423/7/11 had brought discredit upon and reduced confidence in the pharmaceutical industry. The Panel ruled a breach of Clause 2.

A non-contactable complainant who described themselves as a general practitioner complained about advertisements issued by Vifor global which had been the subject of a voluntary admission by Vifor Pharma Limited, Case AUTH/2473/1/12.

In Case AUTH/2473/1/12, Vifor voluntarily admitted that advertisements, published in three specialist European journals, had not been certified prior to publication and the Panel subsequently ruled a breach of Clause 14.1 (it was established that the journals were such that advertisements within them came within the scope of the UK Code). During its consideration of the case, however, the Panel further noted that, as acknowledged by Vifor in subsequent correspondence, the advertisements featured the strapline 'Mastering the art of iron therapy' which had been ruled in breach of Clause 7.2 in Case AUTH/2423/7/11. However, as Vifor's initial voluntary admission only related to a breach of the Code with regard to certification, the Panel could make no ruling with regard to the possible breach of undertaking. Given the importance of complying with undertakings, Vifor was informed of the position and the matter was noted at the end of the published case report. Having read that case report, the complainant now asked for the breach of undertaking to be reinvestigated.

As the complaint concerned an alleged breach of undertaking it was taken up by the Authority in the name of the Director as the Authority was responsible for ensuring compliance with undertakings.

COMPLAINT

The complainant explained that he/she was introduced to the PMCPA website by a medical representative; he/she sometimes read published cases, which he/she found very interesting. The complainant submitted that he/she was surprised by the ruling in Case AUTH/2473/1/12 wherein Vifor made a voluntary admission and was, in the complainant's opinion, treated leniently and ruled in breach of Clause 14.1 only.

The complainant considered that Vifor should also have been ruled in breach of Clauses 25, 9.1 and 2. The complainant was sure that if the advertisement at issue had been placed by a UK company, the PMCPA

would have ruled it in breach of the above clauses. The complainant queried whether the ruling of a breach of Clause 14.1 was because the advertisement in question was placed by the global part of the UK company although, if that was the case, the PMCPA contradicted its own statement in the published case report about it being an established principle that UK companies were responsible for the acts/omissions of overseas parents and affiliates that came within the scope of the Code.

RESPONSE

Vifor explained that it took the Panel's rulings extremely seriously and assured the PMCPA that it was committed to abiding by the Code at all times. Vifor knew the importance of complying with undertakings and the seriousness of the consequences of such a breach for both the company involved and the reputation of the industry as a whole.

Vifor acknowledged that the publication of the advertisements referred to in Case AUTH/2473/1/12 amounted to a breach of the undertaking given in Case AUTH/2423/7/11 and were therefore in breach of Clause 25. Vifor strongly believed in self-regulation hence the voluntary admission in Case AUTH/2473/1/12 as to the failure to certify. Vifor regretted that due to its lack of experience in self-reporting, the breach of Clause 25 was not specifically outlined in its initial letter to the PMCPA and was therefore not formally considered as part of Case AUTH/2473/1/12. Vifor noted, however, that although this was inadvertently not specifically mentioned in its initial letter, a full and frank disclosure acknowledging the breach of Clause 25 in line with the spirit of the Code was included in the follow up letter to the PMCPA in February 2012 prior to the Panel making its ruling. Vifor had now noted the full process for any potential future instances requiring the self-reporting of breaches.

Vifor stated that it had made every effort to ensure compliance with the Authority's ruling in Case AUTH/2423/7/11. All UK materials were withdrawn immediately and its global colleagues were notified that the relevant claims could no longer be used.

Vifor gave details of the steps undertaken to ensure its global colleagues were aware of the relevant ruling as follows:

- August 2011: Notified senior global colleagues of the outcome of the case on the same day the outcome was received by Vifor. This email expressly stated that the claim 'Mastering the art of iron therapy' had been ruled in breach of the Code.
- August 2011: Obtained confirmation of receipt from one of the global colleagues who requested that this topic be discussed at the next global medical directors' meeting.
- September 2011: Case discussed at medical directors' meeting.
- December 2011: Global team trained on ABPI Code.
- February 2012: Training given to global team on inspection training and approval of materials.
- March 2012: Presentation given by senior UK manager to the European Affiliates Board.
- April 2012: Presentation given to global executive operations meeting (Vifor's operational leadership group).

Vifor therefore believed that the actions taken in the UK and globally to notify colleagues of the original undertaking in Case AUTH/2423/7/11, and its self-reporting in Case AUTH/2473/1/12, illustrated that the company took all possible steps to comply and did not fail to maintain high standards. Vifor submitted that it had not breached Clauses 9.1 or Clause 2.

PANEL RULING

The Panel noted that in its consideration of Case AUTH/2473/1/12 it had been extremely concerned to note that the advertisements at issue featured the strapline 'Mastering the art of iron therapy' which was ruled in breach of Clause 7.2 of the Code in Case AUTH/2423/7/11. Vifor had accepted the ruling in that case and provided the relevant undertaking and assurance. Subsequent placement of the advertisements with the same strapline was therefore potentially in breach of the undertaking. The Panel noted that in Case AUTH/2473/1/12 Vifor had voluntarily brought to the Authority's attention advertisements containing the same strapline but had only admitted a breach of the Code with regard to lack of certification. The Constitution and Procedure did not allow the Panel to consider matters which were not subject of a complaint or a voluntary admission and so it had been unable to rule upon the potential breach of undertaking which it had noted and nor was there any mechanism under which it could instigate a fresh complaint. The only option available to the Panel was to point the matter out to the company concerned and note it in the case report. It was very unusual to receive a subsequent complaint about such a matter.

In Case AUTH/2473/1/12 the Panel had noted that a breach of undertaking was a serious matter and it advised Vifor of its concerns which were also noted in the final paragraph of the case report published on the Authority's website in May 2012. The Panel did not refer to any clauses of the Code. The Panel noted that it was this final paragraph of the case report which had appeared to have prompted the complaint now at issue with the complainant citing Clauses 2, 9.1 and 25.

The Panel noted that although the advertisements at issue had been placed by the global organisation in specialist European journals, it was established in Case AUTH/2473/1/12 that advertisements placed in those journals came within the scope of the UK Code. Further, it was an established principle that UK companies were responsible for the acts/omissions of overseas parents and affiliates that came within the scope of the Code.

Turning to Case AUTH/2529/9/12, the Panel noted the repeated use of the claim 'Mastering the art of iron

therapy' and considered that such use breached the undertaking given in Case AUTH/2423/7/11. A breach of Clause 25 was ruled. In that regard high standards had not been maintained. The Panel ruled a breach of Clause 9.1.

The Panel noted the importance of undertakings and considered that failure to comply with the undertaking and assurance previously given in Case AUTH/2423/7/11 had brought discredit upon and reduced confidence in the pharmaceutical industry. The Panel ruled a breach of Clause 2.

Complaint received **17 September 2012**

Case completed **24 October 2012**

CONSULTANT IN PALLIATIVE MEDICINE v PROSTRAKAN

Conduct of representative

A consultant in palliative medicine complained that a representative from ProStrakan, when trying to book an appointment, had inaccurately told his secretary that he and the representative were working together on a symptom control guideline.

The detailed response from ProStrakan is given below.

The Panel noted that the parties' accounts differed with regard to what the representative had stated about the production of the treatment guidelines. The complainant had not been party to the conversation. The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was impossible in such circumstances to determine precisely what had happened.

The Panel noted that the introduction to the Constitution and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities. The complainant had provided no evidence to support his allegation and had accepted that the matter might be a case of miscommunication. The Panel considered that it had not been established that, on the balance of probabilities, the representative's conduct had been in breach of the Code as alleged. No breaches of the Code were ruled.

The Panel noted that ProStrakan had also been asked to consider the requirements of the Code which stated that in seeking appointments, representative must not mislead as to their identity or that of the company they represented. The Panel noted that in this case the complainant and his secretary appeared to be clear as to the representative's identity and that of the company. The Panel ruled no breach of the Code.

A consultant in palliative medicine, complained about the conduct of a representative from ProStrakan UK Ltd.

COMPLAINT

The complainant stated that the representative had tried to arrange an appointment with him via his secretary and that his secretary had been inaccurately told that the complainant and the representative were working together on a symptom control guideline. The complainant apologised if he was mistaken, but he could think of no explanation other than a deliberate attempt to mislead. The complainant, therefore, queried whether there had been a breach of the Code.

When writing to ProStrakan, the Authority asked it to respond in relation to Clauses 9.1, 15.2 and 15.5 of the Code.

RESPONSE

ProStrakan submitted that it took its responsibilities under the Code very seriously and on receipt of the complaint it immediately investigated the complainant's concerns. The representative and his manager were both interviewed. The interviews indicated that the representative met the complainant's secretary in September 2012 in order to book a meeting with the complainant. However, at no point during their conversation did the representative claim that he (or any other ProStrakan employee) was working with the complainant on a symptom control guideline as alleged. The representative mentioned the guideline in question but only in order to explain that he wished to offer the complainant up-to-date product information on Abstral (fentanyl citrate).

ProStrakan submitted that the representative had contacted the secretary as he had been informed that this was the correct way in which to book an appointment with the complainant. The representative had not yet met the complainant but had heard that he was putting together guidelines on pain management in palliative care. As the complainant worked for a palliative care service and ProStrakan had a product in this therapy area, the representative wished to contact the complainant in order to ensure that he had the most current information on Abstral.

On arriving at the building in which the complainant and his secretary worked, the representative introduced himself to the receptionist and asked if it would be possible to talk to the secretary. The receptionist rang the secretary who came down to the reception area to talk to him. The representative introduced himself and stated that he was a representative from ProStrakan. He produced his business card and asked if it would be possible to make an appointment to see the complainant; he explained that he had heard that the complainant was working on pain guidelines and that he wished to offer him up-to-date product information on Abstral. The secretary stated that it was not possible to book an appointment with the complainant and so the representative asked if there was another way to contact him. In response to this the secretary offered her own email address and stated that she would pass any information provided on to the complainant.

The representative's manager was present during this conversation as he was on a field visit that day. The above account was corroborated by the manager who was interviewed separately. When questioned directly regarding the representative's conduct with customers, the manager stated that he had never had any concerns in this regard despite having managed the representative for five years.

During the interviews both employees were asked about what had specifically been said during the conversation about the production of treatment guidelines. Both replied that the guidelines had been mentioned but only in the context described above. Neither employee claimed to have been involved in the production of the guidelines, or to have worked on them in collaboration with the complainant. The conversation in question lasted only a few minutes, after which both employees left. No emails had been exchanged with the complainant's secretary.

ProStrakan stated that it did not produce specific written instructions to representatives about asking for appointments. All ProStrakan representatives were observed regularly on field visits by their manager to ensure that high standards were maintained at all times.

Whilst ProStrakan respected the complainant's view, and thanked him for taking the time to discuss the issue, it believed that the complaint in this case had arisen from a miscommunication. ProStrakan assured the complainant that, while it appeared that a miscommunication had occurred, there was never a deliberate attempt to mislead.

Given the account of the conversation above, ProStrakan submitted that the representative had acted in accordance with the Code and had at all times maintained high standards. The company denied breaches of Clauses 9.1 and 15.2.

ProStrakan submitted that when he introduced himself to the complainant's secretary, the representative took all reasonable steps to ensure that he was clear as to who he was and why he wished to book an appointment with the complainant. A business card was produced in order to further clarify these details. ProStrakan thus denied a breach of Clause 15.5.

FURTHER COMMENTS FROM THE COMPLAINANT

In response to a request for comments upon ProStrakan's submission, the complainant stated that on speaking to his secretary and the receptionist, both stood by their accounts of the meeting with the representative. The complainant stated that ProStrakan's suggestion that this was an example of miscommunication therefore seemed reasonable in that the two groups clearly had different recollections of what was said. The complainant noted, however, that as the conversation was not recorded, there could only be speculation as to what was said.

PANEL RULING

The Panel noted that the parties' accounts of what the representative had stated with regard to the production of the treatment guidelines differed. The complainant had not been party to the conversation. The complainant had been sent a copy of ProStrakan's submission and on speaking to his secretary and the receptionist, they both stood by their version of events. The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was impossible in such circumstances to determine precisely what had happened.

The Panel noted that the introduction to the Constitution and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities. The complainant had provided no evidence to support his allegation and had accepted that the matter might be a case of miscommunication. The Panel considered that it had not been established that, on the balance of probabilities, the representative's conduct had been in breach of the Code as alleged. The Panel thus ruled no breach of Clauses 9.1 and 15.2.

The Panel noted that ProStrakan had also been asked to consider the requirements of Clause 15.5 which stated that in seeking appointments, representative must not mislead as to their identity or that of the company they represented. The Panel noted that in this case the complainant and his secretary appeared to be clear as to the representative's identity and that of the company; ProStrakan had submitted that the representative had used his business card. The Panel ruled no breach of Clause 15.5.

Complaint received **19 September 2012**

Case completed **6 November 2012**

CASE AUTH/2533/10/12

ANONYMOUS v BAYER

Representative call rates

Someone who appeared to be a Bayer employee complained anonymously that Bayer HealthCare's incentive scheme for representatives encouraged three calls/visits on all target customers in the second half of the year regardless of previous activity. Part of a presentation detailing the scheme was submitted.

The detailed response from Bayer is given below.

The Panel noted that the Code stated that the number of calls made on a doctor or other prescriber each year should normally not exceed three on average excluding attendance at group meetings and the like, a visit requested by the doctor or other prescriber or a visit to follow up an adverse reaction report. Thus, although a representative might proactively call on a doctor or other prescriber three times in a year, there might be more than three contacts with that health professional in the year. Briefing material should clearly distinguish between expected call rates and expected contact rates. Targets should be realistic and not such that representatives breached the Code in order to meet them.

The Panel noted that the presentation at issue, Incentive Scheme H2 2012, and a second presentation relating to the consolidated objectives of the incentive schemes were emailed to representatives. The covering email referred to the current sales performance. The email did not refer to the Code or its requirements in relation to representatives calling on doctors and other prescribers.

The H2 incentive scheme had been introduced to deliver sales. The bonus pool per representative available for the second half of 2012 for 'on target' performance was stated; higher bonus payments could be achieved for overperformance.

The scheme was active July - December 2012, but coverage and frequency commenced in June. To achieve the highest bonus representatives had to see 80% of target customers at least once. Representatives were also rewarded if they saw 50% of target customers three times with a sliding scale for coverage below that.

The final slide of the presentation noted that the terms and conditions for the pre-existing H1 incentive scheme remained in effect and in case of questions a representative should contact his/her line manager. As with the covering email, the presentation did not refer to the Code or its requirements in relation to representatives calling on doctors and other prescribers.

The second presentation, sent to representatives with the one at issue and entitled 'Consolidation Objectives for H2', began by outlining the sales targets to be achieved by the end of 2012. The national expectations for the primary care representatives was that, *inter alia*, they would see 50% of target customers three times (or more including call backs or requests for visits), with 80% to be seen at least once between June and December 2012.

The Panel noted Bayer's submission that the presentation at issue made it clear that the terms and conditions for the H1 incentive scheme remained in effect. Bayer had submitted a document '2012 Primary Care Incentive Scheme including Terms & Conditions' dated March 2012. The document did not refer to any specific requirements of the Code or company standard operating procedures (SOPs) in relation to the frequency of calls on doctors or other prescribers.

The Panel noted Bayer's submission that as a result of sales force questions about the H2 incentive scheme a document detailing frequently asked question (FAQs) was produced and certified in September. One question was 'Having seen some contacts once or twice already this year, seeing them another three times is a challenge, especially when many don't attend meetings. Is conducting four to five unsolicited calls a year compliant?', to which the answer was 'You do need to ensure that you are conducting your activity within the limit of 3 unsolicited calls per year'. The Panel was concerned that this appeared to be the only reference to the requirements of the Code in relation to call rates in any of the material relating to both the H1 and H2 incentive schemes.

The Panel noted Bayer's submission that the sales force was provided with its SOP ' The ABPI Code of Practice for Representatives', which stated, *inter alia*, that representatives could only make three promotional calls per year on an individual prescriber. Contacts made at meetings and visits made in response to a request from the prescriber were in addition to the three proactive calls. In addition, a presentation given at the initial training course for all representatives referred, *inter alia*, to this SOP and stated 'Calls are proactive – no more than 3 per [health professional] per year'.

The Panel noted Bayer's submission that, with the benefit of hindsight, the requirements of the Code in relation to call rates could have been clearer in the presentation at issue. The Panel noted that neither the presentation nor the briefing material about the H2 incentive scheme referred to the specific requirements of the Code in relation to call rates.

Although initial representative training covered these requirements the Panel considered that the material about the H2 incentive scheme, including the presentation in question, should be capable of standing alone in relation to compliance with the Code. An FAQ document provided some explanation but this was produced some two months after the initial briefing on the H2 incentive scheme.

The Panel considered that the material in question advocated a course of action which was likely to breach the Code and in that regard the material did not maintain a high standard. Breaches of the Code were ruled. The Panel noted that the Code required representatives to ensure that, *inter alia*, the frequency of their calls on health professionals did not cause inconvenience. No evidence had been submitted to establish a breach in this regard and thus no breach of the Code was ruled.

The Panel noted that initial training and an internal SOP did refer to the requirements of the Code. Whilst the Panel was very concerned about the material at issue as reflected in its comments and rulings above, on balance, it considered that the circumstances did not warrant a ruling of a breach of Clause 2, which was reserved as a sign of particular censure. No breach of that clause was ruled.

Someone who appeared to be an employee of Bayer complained anonymously about Bayer HealthCare's incentive scheme for representative calls. The complainant was non-contactable.

COMPLAINT

The complainant provided a copy of slides about the incentive scheme and alleged a breach of the Code as the scheme encouraged three calls/visits on all target customers in the second half of the year regardless of previous activity.

The complainant highlighted certain sections of the slides. In relation to primary care, firstly that the scheme was active from 1 July until 31 December with coverage and frequency to start on 1 June.

The second section highlighted related to the activity of the primary care team:

- **Frequency activity scale:**
  - 50% * 3 visits on target customers = £[X]
  - 45% * 3 visits on target customers = £[Y] amounts stated
  - 40% * 3 visits on target customers = £[Z]

There was no explanation for the asterisk.

The complainant highlighted two sections from the key account manager (KAM) presentation:

Firstly,

- Scheme Active from July 1st – December 31st
  - Coverage and frequency to commence 1st June
- Inputs Paid at Year End 2012
- Outputs Paid Quarterly

Secondly,

- **Frequency activity scale:**
  - 75% * 3 visits on target customers = £[X]
  - 65% * 3 visits on target customers = £[Y] amounts stated
  - 55% * 3 visits on target customers = £[Z]

Again there was no explanation for the asterisk.

When writing to Bayer, the Authority drew attention to Clauses 2, 9.1, 15.4 and 15.9 of the Code.

RESPONSE

Bayer HealthCare stated that the incentive scheme was launched after a review of sales force performance during the first half of 2012. It was concluded that a greater focus on sales representatives' activity was required. The H2 incentive scheme was adjusted to increase coverage of customers in accordance with the revised objectives.

Bayer submitted that the attachment accompanying the complaint was an incomplete copy of a presentation regarding an incentive scheme H2 2012. The introductory slides had not been included. The complete presentation, 'Incentive Scheme H2 2012', was emailed to the sales force together with a document 'Consolidated Objectives for H2', as briefing materials in late July. The incentive scheme was active from July to December 2012 but included coverage and frequency from June 2012. The presentation made it clear that the terms and conditions for the H1 incentive scheme, as outlined in the briefing document '2012 Primary Care Incentive Scheme including Terms and Conditions', remained in effect. The briefing document had the following statements:

- Introduction & Scheme Details – 'The scheme helps to drive performance in a manner that meets with the requirements of the ABPI Code of Practice and internal SOPs'

- 2012 Objectives – 'Focus on Corporate Governance, the ABPI Code of Practice and "Hitting The Numbers" in the Right Way'

- Eligibility – 'Employees who breach any company policy or ABPI Code of Practice that leads to formal disciplinary action will have their "Hitting the Numbers" scheme payments reviewed and reduced/stopped in accordance with company guidelines'

Members of the sales force were asked to sign the briefing document to indicate that they had read, understood and agreed to the terms and conditions. The covering email to which the briefing materials were attached instructed the sales force to speak to their line manager if they had any queries.

Bayer submitted that sales force questions were collated and discussed by senior managers at weekly teleconferences in July/August 2012. As a result a draft frequently asked questions (FAQ) document

was distributed in August 2012. The final FAQ was certified in late September 2012 and included the following two questions about coverage and frequency:

1 Question – 80% coverage with a frequency of three on target customers is usually a target given at the beginning of the year, is this objective achievable at this point in the year?

Answer – The objective is to see 50% of target customers x 3 (or more including call backs or requests for visits), 80% to be seen at least once from 1st June to 31st December 2012. Conducting meetings will support this as meetings often provide an opportunity for a planning call, a call at the meeting itself and then a follow up call.

N.B. A Call back is defined as a visit which is requested by a doctor or other prescriber or a call that is made in order to respond to a specific enquiry.

2 Question – Having seen some contacts once or twice already this year, seeing them another three times is a challenge, especially when many don't attend meetings. Is conducting four to five unsolicited calls a year compliant?

Answer – You do need to ensure that you are conducting your activity within the limit of three unsolicited calls per year.

Bayer stated that the importance of not exceeding the maximum number of proactive calls and inconveniencing health professionals was emphasized in sales force training. All attended an initial training course (ITC) and engaged in continuing training for Code compliance and adherence with Bayer standard operating procedures (SOPs). The SOP 'The ABPI Code of Practice for Representatives' was provided together with the ITC presentation 'BHP SOP Training for New Starters, Field Force' and a copy of the sales force training record 'GM Sales Wellards training'.

With regard to Clause 15.9, Bayer submitted that the relevant enclosures were satisfactory. It was never Bayer's intention to encourage the sales force to exceed a maximum of three proactive calls on an individual health professional. Although this point and the importance of compliance was emphasized in training and other materials, with the benefit of hindsight, this could have been made clearer in the presentation 'Incentive Scheme H2 2012' distributed in July 2012.

In order to ensure that no more than three proactive calls were made on an individual health professional (Clause 15.4), all representatives kept a real time record of their calls on iPads via the electronic customer relationship management system. Call rates were frequently monitored by the sales leadership team.

Bayer did not believe that it had brought the industry into disrepute (Clause 2) or failed to maintain high standards (Clause 9.1). In support of this submission Bayer stated that no health professionals had complained that they had been inconvenienced by calls from the sales force.

PANEL RULING

The Panel noted that the supplementary information to Clause 15.4 stated that the number of calls made on a doctor or other prescriber each year should normally not exceed three on average excluding attendance at group meetings and the like, a visit requested by the doctor or other prescriber or a visit to follow up a report of an adverse reaction. Thus although a representative might proactively call on a doctor or other prescriber three times in a year, the number of contacts with that health professional in the year might be more than that. The supplementary information advised that briefing material should clearly distinguish between expected call rates and expected contact rates. Targets should be realistic and not such that representatives breached the Code in order to meet them.

The Panel noted that the presentation at issue, 'Incentive Scheme H2 2012' (ref UK.PH.GM.2012.057), and a second presentation relating to the consolidated objectives of the incentive schemes (ref UK.PH.GM.2012.055) were emailed to representatives. The covering email referred to the current sales performance and noted, *inter alia*, that:

> 'It is now vital that you, who are in critical customer facing roles, are freed up to maximise the number of target customers seen during the second half of 2012' and
>
> 'There is nothing more important than your time on territory, the number of target customers you see and your effectiveness in each call you make. The conclusions are very clear in the objectives outlined in the H2 objectives document'

There was no mention in the email of the Code or its requirements in relation to representatives calling on doctors and other prescribers.

The Panel noted that the complete presentation in question submitted by Bayer explained that the H2 incentive scheme had been introduced to deliver sales. The presentation explained the ratio of outputs (sales) and inputs (activities and projects) required and stated the bonus pool per representative (primary care, key account managers (KAMs) and healthcare development managers (HDMs)) available for the second half of 2012 for 'on target' performance. Higher bonus payments could be achieved for overperformance. This was not quantified. The incentive schemes for the HDMs, primary care teams and KAMs and RBMs were then outlined.

The presentation noted that 40% of each primary care representative's incentive would be paid on inputs and 60% on outputs. The scheme was active from 1 July until 31 December 2012, but coverage and frequency commenced on 1 June. To achieve the highest bonus representatives had to see 80% of target customers at least once and for less coverage

there was a sliding scale of reduced payments. Each team had to achieve at least 40% coverage to qualify for any bonus. Representatives were also rewarded if they saw 50% of target customers three times with a sliding scale for coverage below that. Each team had to see at least 25% of target customers three times to qualify for any bonus. The incentive scheme for the KAMs was similar.

The final slide of the presentation was entitled 'Terms and Conditions' and noted that the terms and conditions for the pre-existing H1 incentive scheme remained in effect and in case of questions a representative should contact his/her line manager. As with the covering email, the presentation did not refer to the Code or its requirements in relation to representatives calling on doctors and other prescribers.

The second presentation which was sent to representatives with the one at issue was entitled 'Consolidation Objectives for H2' and began by outlining the sales targets to be achieved by the end of 2012. It noted, *inter alia*, the expectations for the primary care team and the KAMs. The national expectations for the primary care representatives was that, *inter alia*, they would see 50% of target customers three times (or more including call backs or requests for visits), with 80% to be seen at least once between 1 June and 31 December 2012. The slide covering the expectations of the KAM team covered the administrative expectations, meeting expectations and compliance expectations. The latter required, *inter alia*, a thorough knowledge of the Code and other appropriate guidelines including company SOPs, although no specific requirements were referred to.

The Panel noted Bayer's submission that the presentation at issue made it clear that the terms and conditions for the H1 incentive scheme remained in effect. Bayer had submitted a document '2012 Primary Care Incentive Scheme including Terms & Conditions' (ref UK.PH.GM.X.2012.055c) dated March 2012. It appeared that this document related to the general medicine team, although it was unclear whether it applied to the KAMs. The introduction stated that the scheme helped to drive performance in a manner that met with the requirements of the Code and internal SOPs. The objectives section required representatives to, *inter alia*, focus on corporate governance, the Code and 'Hitting The Numbers' in the right way. The document did not refer to any specific requirements of the Code or company SOPs in relation to the frequency of calls on doctors or other prescribers.

The Panel noted Bayer's submission that as a result of sales force questions about the H2 incentive scheme an FAQ document was produced and certified on 27 September (ref UK.PH.GM.2012.079). One question in the primary care representative section was '80% coverage with a frequency of 3 on target customers is usually a target given at the beginning of the year, is this objective achievable at this point in the year?'. The answer provided was 'The objective is to see 50% of target customers x 3 (or more including call backs or requests for visits), 80% to be seen at least once from 1st June to 31st December 2012. Conducting meetings will support this as meetings often provide an opportunity for a planning call, a call at the meeting itself and then a follow up call. On most territories there are [X] [primary care representatives] and there is also the support provided by the KAM's via the meeting in a box objective in order to drive the frequency that it required'.

A further question, which appeared in the KAM section of the FAQ document, was 'Having seen some contacts once or twice already this year, seeing them another three times is a challenge, especially when many don't attend meetings. Is conducting four to five unsolicited calls a year compliant?', to which the answer was 'You do need to ensure that you are conducting your activity within the limit of 3 unsolicited calls per year'. The Panel was concerned that this appeared to be the only reference to the requirements of the Code in relation to call rates in any of the material relating to both the H1 and H2 incentive schemes.

The Panel noted Bayer's submission that all of the sales force were provided with its SOP 'The ABPI Code of Practice for Representatives' (BHC-BP-UK-SOP-117) which stated in section 3.2.1.2, Call Frequency, *inter alia*, that representatives could only make three promotional calls per year on an individual prescriber. Contacts made at meetings and visits made in response to a request from the prescriber were in addition to the three proactive calls. In addition, a presentation given at the initial training course for all representatives (ref UK.PH.MG.2012.016), *inter alia*, referred to this SOP and stated 'Calls are proactive – no more than 3 per [health professional] per year'.

The Panel noted Bayer's submission that, with the benefit of hindsight, the requirements of the Code in relation to call rates could have been clearer in the presentation at issue. The Panel noted that neither the presentation in question nor the briefing material in relation to the H2 incentive scheme referred to the specific requirements of the Code in relation to call rates. Although initial representative training covered these requirements the Panel considered that the material about the H2 incentive scheme, including the presentation in question, should be capable of standing alone in relation to compliance with the Code. An FAQ document provided some explanation, however this was produced some two months after the initial briefing on the H2 incentive scheme.

The Panel considered that the material in question advocated a course of action which was likely to breach the Code. A breach of Clause 15.9 was ruled. The Panel noted that Clause 15.4 required representatives to ensure that, *inter alia*, the frequency of their calls on health professionals did not cause inconvenience. No evidence had been submitted to establish a breach of this clause and thus no breach of Clause 15.4 was ruled.

The Panel considered that by advocating a course of action which was likely to breach the Code, the material at issue did not maintain a high standard and a breach of Clause 9.1 was ruled.

The Panel noted that initial training and an internal SOP did refer to the requirements of the Code. Whilst the Panel was very concerned about the material at issue as reflected in its comments and rulings above, on balance it considered that the circumstances did not warrant a ruling of a breach of Clause 2, which was reserved as a sign of particular censure. No breach of that clause was ruled.

Complaint received **11 October 2012**

Case completed **27 November 2012**

ANONYMOUS v ROCHE

Alleged inducement to continue with project

An anonymous, non-contactable complainant alleged that Roche had brought pressure to bear on a named hospital employee to continue with a project in rheumatoid arthritis. The complainant alleged that drinks and money were provided which was not right.

The detailed response from Roche is given below.

The Panel noted that, as set out in the introduction to the Constitution and Procedure, complainants had the burden of proving their complaint on the balance of probabilities. Anonymous complaints were accepted and, like all complaints, judged on the evidence provided by the parties. The complainant had submitted no material to support his/her position and the Panel was unable to obtain more information or comment upon Roche's response. The Panel noted the difficulty of dealing with complaints based on one party's word against the other.

The Panel had to make a ruling on the evidence before it. The complainant had not provided any evidence to substantiate his/her allegation. Roche's investigation of the matter did not reveal any evidence to show that the company had provided any inducements in the form of inappropriate payments or hospitality. On the contrary, the company had contacted the named hospital employee who had confirmed that no pressure had been exerted and no inducements offered. The Panel thus ruled no breach of the Code including no breach of Clause 2.

An anonymous, non-contactable complainant, who appeared to work within a named hospital group, complained about the activities therein of Roche Products Limited.

COMPLAINT

The complainant alleged that Roche had breached Clause 2 in the work it had done in the hospitals. The hospital group had declined to participate in the company's project about rheumatoid arthritis and remission data analysis with a named hospital employee. Roche had exerted pressure on that employee to continue. The complainant also alleged that drinks and money were provided by Roche and this was not right. The complainant stated that a named Roche employee was responsible.

When writing to Roche, the Authority asked it to respond in relation to Clauses 9.1, 18.1 and 19.1 in addition to Clause 2 as cited by the complainant.

RESPONSE

Roche submitted that it currently had no projects running with the named hospital employee. That employee was a pharmacist who also had a business outside his hospital employment and it was with this company that Roche worked between July and September 2012 to develop a model to assess the cost of remission/low disease activity vs non-remission/high disease activity in rheumatoid arthritis (a copy of the brief was provided). The project was led by a temporary contract employee who left Roche at the end of September. Whilst progressing this, as a supplier to Roche, the pharmacist questioned Roche's policy that all contracts with health professionals, and ultimately all payments, were with and by Roche directly; this was to ensure the company's ability to report all payments, made by Roche and third parties working on its behalf. Roche advised the pharmacist that its process must be followed. The pharmacist explained this to the health professionals, who in turn understood that this work was for and on behalf of a pharmaceutical company and chose not to participate. As a result, the project was not progressed. To the best of its knowledge Roche had not carried out any other projects with the pharmacist or his company.

Roche explained that the employee named by the complainant worked in Roche's marketing department and the only interaction he/she had had with the pharmacist was a teleconference on 19 September. Roche's contract employee led the discussion. The named Roche employee's only contribution to the meeting was at the end to stress to the pharmacist that he/she would be his point of contact after the contract employee left Roche. The named employee had had no further discussion or contact with the pharmacist and strenuously denied that he/she had met the pharmacist, had exerted pressure on him or had offered drinks or money to be involved in a project.

Roche stated that a search of Zinc showed no agreements in place between it and the pharmacist or his company and a search of the meetings and hospitality approval system showed no meetings or hospitality associated with the pharmacist or his company. Similarly the sponsorship request system showed no sponsorships being approved or paid to the pharmacist or his company and none of the named employee's expenses related to the pharmacist or his company and in relation to the contract employee whose expenses were paid via a third party, no such expenses were evident.

Roche had contacted the pharmacist who confirmed that Roche had been professional in its dealings with him and his company in terms of discussions and he had never been put under any pressure, in fact he would argue the opposite. Discussions had been through his company and no inducements had been offered. Financial agreements were based on

consultancy through his company not as an individual or as a member of the NHS and other inducements, such as drinks had never been offered or accepted. His only dealing with the Roche employee was via a teleconference to which he/she was just one of the parties.

In conclusion Roche submitted that there was no evidence to support the anonymous allegations and it denied any breach of Clauses 2, 9.1, 18.1 or 19.1.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable and that, as set out in the introduction to the Constitution and Procedure, complainants had the burden of proving their complaint on the balance of probabilities. Anonymous complaints were accepted and, like all complaints, judged on the evidence provided by the parties. The complainant had submitted no material to support his/her position and the Panel was unable to contact him/her to ask for more information or for comment upon Roche's response. The Panel noted the difficulty of dealing with complaints based on one party's word against the other.

The Panel had to make a ruling on the evidence before it. The complainant had not provided any evidence to substantiate his/her allegation. Roche's investigation of the matter did not reveal any evidence to show that the company had provided any inducements in the form of inappropriate payments or hospitality. On the contrary, the company had contacted the pharmacist who had confirmed that no pressure had been exerted and no inducements offered. The Panel thus ruled no breaches of Clauses 18.1 and 19.1. The Panel consequently ruled no breach of Clauses 9.1 and 2.

Complaint received **12 October 2012**

Case completed **5 December 2012**

ANONYMOUS v BAYER

Promotion of Xarelto

An anonymous, non-contactable complainant complained about a two page advertisement published in GP, 24 October 2012, for Xarelto (rivaroxaban) issued by Bayer HealthCare. Xarelto was an oral anticoagulant. The advertisement referred, *inter alia*, to the use of Xarelto for stroke prevention in atrial fibrillation (AF) and in that regard stated 'one tablet, once daily, simple'.

The complainant's view was that the advertisement was outrageous. Xarelto, like all anticoagulants, carried a risk of bleeding which could be severe or even fatal. The use of all anticoagulants needed to be considered and monitored with care.

The claim that Xarelto was 'simple' to use did not accurately reflect the inherent risks with this class of medicine nor was it consistent with the prescribing information which did not seem to support that this was a simple medicine to use. There were cautions and/or dose reductions in renal impairment and the 'Contraindications', 'Warnings and Precautions' and 'Interactions' sections were extensive, complex and covered a wide range of situations and circumstances.

The complainant alleged that advertising the use of such a medicine as 'simple' was likely to encourage inadequately considered or even inappropriate use with a consequent impact on patient safety.

The detailed response from Bayer is given below.

The Panel noted that it was clear that the reference to simple was in relation to the indication for stroke prevention in AF. It was also clear that 'simple' referred to the dosing regimen, as it appeared in the phrase 'one tablet, once daily, simple'. It was not a claim that generally Xarelto was simple to use.

The Panel considered that readers of the advertisement (GPs and health professionals working in primary care) would be aware of the complexities associated with the use of warfarin. It noted Bayer's submission regarding the need to monitor and adjust the doses of warfarin. Sections 4.4 and 5.1 of the Xarelto 20mg summary of product characteristics (SPC) stated that there was no need for the monitoring of coagulation parameters during treatment with rivaroxaban in clinical routine. However, if clinically indicated, rivaroxaban levels could be measured by certain tests. Section 4.4 of the SPC stated that 'Clinical surveillance in line with anticoagulation practice is recommended throughout the treatment period'.

The Panel noted the recommended dose of Xarelto in the prevention of stroke and systemic embolism in patients with AF and certain risk factors was 20mg per day. Therapy was to be continued long-term provided the benefit of prevention of stroke and systemic embolism outweighed the risk of bleeding. Dose adjustment was needed in patients with renal impairment.

The Panel did not consider there was a general claim that Xarelto was simple to use as alleged. 'Simple' was used to describe the dosing regimen. The dosing regimen for Xarelto was not as complicated as for other products in this therapeutic area and in this context the broad indication of one tablet once a day for a number of patient populations might be viewed as simple.

The Panel did not consider that the claim 'one tablet, once daily, simple' was inconsistent with the SPC. Nor was the claim an inaccurate reflection of the risks of using anticoagulants as alleged. Given the above the Panel did not consider the company had failed to maintain high standards nor had it brought discredit to or reduced confidence in the pharmaceutical industry. No breaches of the Code, including no breach of Clause 2, were ruled.

An anonymous, non-contactable complainant complained about a two page advertisement (ref L.GB.09.2012.0568h) for Xarelto (rivaroxaban) issued by Bayer HealthCare. Xarelto was an anticoagulant. The advertisement, which was published in GP, 24 October 2012, referred, *inter alia*, to the use of Xarelto for stroke prevention in atrial fibrillation (AF) and in that regard stated 'one tablet, once daily, simple'.

COMPLAINT

The complainant stated that in his/her view the advertisement was outrageous. Xarelto was an oral anticoagulant which, like all anticoagulants, carried an attendant risk of bleeding which could be severe or even fatal. The use of all anticoagulants needed to be considered and monitored with care.

The complainant noted that the advertisement indicated that Xarelto was 'simple' to use which, in his/her view, did not accurately reflect the inherent risks with this class of medicine nor was it consistent with the prescribing information. The prescribing information certainly did not seem to support that this was a simple medicine to use. There were cautions and/or dose reductions in renal impairment and the 'Contraindications', 'Warnings and Precautions' and 'Interactions' sections were very extensive, quite complex and covered a wide range of situations and circumstances.

The complainant alleged that advertising the use of such a medicine as 'simple' was likely to encourage

inadequately considered or even inappropriate use with consequent impact on patient safety.

When writing to Bayer, the Authority asked it to consider the requirements of Clauses 2, 3.2, 7.2, 7.9 and 9.1.

RESPONSE

Bayer explained that before the introduction of this latest class of anticoagulants, referred to in the literature as novel oral anticoagulants (NOACs), there were two main treatment options, injectable anticoagulants such as heparin and oral medicines vitamin K antagonists like warfarin.

Heparins required dose adjustment by weight and needed to be administered at least once a day. Injections might result in extensive bruising, stress of needle prick, pain and discomfort. Self-injection required dexterity which not all older patients had, so help from a carer or visit by a district nurse was necessary. In addition, sharps and needles had to be disposed of properly.

Bayer submitted that vitamin K antagonists had a number of limitations including a narrow therapeutic index which required monitoring of the international normalised ratio (INR) and adjustment of the dose accordingly. There were three tablet strengths (1mg, 3mg, 5mg) which had to be used in various combinations in order to administer the required dose. This could be a source of dose error as noted in the Rapid Response Report (NPSA/2010/RRR018), 'Preventing fatalities from medication loading doses'. The report 'Medication involved in reported incidents' listed warfarin as the first of four critical medicines linked to loading dose errors.

Bayer stated that the dose of warfarin needed to be adjusted to take account of changes in food, drinks and concomitant medicines (warfarin summary of product characteristics (SPC)). Travelling and holidays might also be a concern and the majority of patients who had to attend clinics regularly for monitoring might find it difficult. Such considerations would have an impact on life style.

Bayer agreed with the complainant's comment that the use of all anticoagulants needed to be considered and monitored with care. Sections 4.4 and 5.1 of the Xarelto SPCs stated that 'There is no need for the monitoring of coagulation parameters during treatment with rivaroxaban in clinical routine. However, if clinically indicated rivaroxaban levels can be measured by calibrated quantitative anti-Factor Xa tests'. This was in marked contrast to warfarin which required regular monitoring of a patient's INR as part of the clinical routine.

Bayer submitted that the recommended dose for prevention of stroke and systemic embolism was 20mg once a day which was also the recommended maximum dose. Although the initial treatment of deep vein thrombosis (DVT) was 15mg twice a day for three weeks thereafter the dose was 20mg once a day. Bayer maintained that once a day dosing which did not need adjusting in patients, other than those with moderate to severe renal impairment, was simple. Simple did not imply that there was no risk of adverse events. However, it might be that once a day dosing, without the need for dose adjustment in the vast majority of patients, was more likely to result in patients being appropriately anticoagulated compared with warfarin. Bayer noted that even patients optimally treated with warfarin would only have an INR of 2-3 for approximately 60-70% of the time.

Bayer submitted that there were fewer interactions for Xarelto than warfarin with other medicines, food and drink.

Bayer stated that the advertisement made it clear that the indications for which Xarelto was to be used were DVT treatment and stroke prevention in AF which was consistent with the SPC. Furthermore, prominence was given to the indications for Xarelto recommended by NICE.

In addition to the above, Bayer also noted that the Atrial Fibrillation Association (patient organisation), the European Society of Cardiology (ESC) and clinicians with an interest in anticoagulation considered that the class of medicine to which Xarelto belonged was easier to manage, offered convenience and was simple.

Bayer noted that the Atrial Fibrillation Association's patient booklet, published in 2008 for individuals affected by atrial fibrillation and endorsed by the Department of Health, stated that 'Warfarin remains a popular and very effective drug at reducing the risk of stroke in high risk patients with atrial fibrillation. However, these new options offer some advantages. They do not need regular blood monitoring, they are more stable, having far fewer interactions with food, drinks and medications than warfarin and so [sic] easier to manage, the new oral anticoagulants are affective [sic] almost immediately after taking, and large clinical trials have shown them to be as effective as warfarin in reducing the risk of stroke'.

The 2012 focused update of the ESC Guidelines for the management of atrial fibrillation included the following key point 'The NOACs offer better efficacy, safety, and convenience compared with [oral anticoagulation] with [vitamin K antagonists]. Thus, where an oral anticoagulant is recommended, one of the NOACs – either a direct thrombin inhibitor (dabigatran) or an oral factor Xa inhibitor (eg rivaroxaban, apixaban) – should be considered instead of adjusted-dose vitamin K antagonist (INR 2–3) for most patients with AF'.

Bayer quoted the following from published literature:

- Mousa (2010).

  'Rivaroxaban represents a potentially attractive alternative to warfarin, as it could enable simplified once-daily dosing, requires no therapeutic monitoring, and has a lower potential for drug interactions.'

- Buller (2010).

  'New oral anticoagulants hold the promise of simple fixed-dose regimens without the need for monitoring and could make extended use more attractive.'

- Ru San *et al* (2012).

  'With convenient fixed-dose administration, the NOACs facilitate anticoagulant management in AF in the community, which has hitherto been grossly underutilised. Guidelines should evolve towards simplicity in anticipation of greater use of NOACs among primary care physicians.'

- Buller and Darius (2010).

  'Against a background of prolonging anticoagulant treatment for many months to years, this study indicates that oral rivaroxaban, 15mg twice-daily for 3 weeks followed by 20mg once-daily, could provide clinicians and patients with a simple, single-drug approach for the acute and continued treatment of DVT that potentially improves the benefit-risk profile of anticoagulation.'

- Bauersachs *et al* (2010).

  'Rivaroxaban offers a simple, single-drug approach to the short-term and continued treatment of venous thrombosis that may improve the benefit-to-risk profile of anticoagulation.'

- Bauer (2011).

  'Rivaroxaban offers a simple and convenient single-drug oral approach to the initial treatment of venous thrombosis; this approach is also being tested with apixaban.'

- Cohen and Dobromirski (2012).

  'Moreover, the simple, once-daily oral administration of rivaroxaban could potentially improve adherence to extended-duration VTE treatment compared with the current standard of care in individuals with confirmed DVT or PE [pulmonary embolism].'

- Turpie (2012).

  'This article provides an overview of the phase III clinical development programmes for these novel OACs, with special focus on rivaroxaban. With encouraging data already emerging, the promise of a simplified single-drug approach for VTE treatment is on the horizon.'

- Mills *et al* (2012).

  'Initiating rivaroxaban approximately 12 or 24 hours after the last LMWH [low molecular weight heparin] dose (as appropriate) provides simple, well-tolerated transition strategy for thromboprophylaxis in patients undergoing THR [total hip replacement]/TKR [total knee replacement] surgery.'

- Bates and Weitz (2008).

  'Its rapid onset of action appears to eliminate the need for initial overlap with a parenteral anticoagulant like low-molecular-weight heparin, whereas its rapid offset of action should simplify management in the case of hemorrhage or the need for intervention.'

- Tagarakis *et al* (2010).

  'Many researchers have until now united their efforts in the endeavour to discover new anticoagulants, which would be simpler to use and safer to administer, so that patients would avoid both thromboembolic events as well as life threatening episodes of bleeding. One of these agents, that is hereby presented along with patents, is dabigatran, which promises much for the future, despite the fact that time and the awaited results of ongoing trials will be necessary for its establishment as a first-line anticoagulant. More specifically, based on the major trials of RELY and RECOVER, we could state that dabigatran has presented satisfactory outcomes in terms of bleeding and prevention of venous thromboembolism.'

In conclusion Bayer contended that Xarelto was simple and that this view was an accurate, fair, objective and unambiguous reflection of the literature. Consequently, Bayer considered that the advertisement at issue did not breach of Clauses 2, 3.2, 7.2, 7.9 or 9.1 of the Code.

PANEL RULING

The Panel noted the advertisement stated 'Xarelto for stroke prevention in AF, one tablet, once daily, simple'. It was clear that the reference to simple was in relation to the indication for stroke prevention in AF. It was also clear that 'simple' referred to the dosing regimen, as it appeared in the phrase 'one tablet, once daily, simple'. It was not a claim that generally Xarelto was simple to use.

The Panel agreed that the use of anticoagulants was complex. It considered that readers of the advertisement (GPs and health professionals working in primary care) would be aware of the complexities associated with the use of warfarin. It noted Bayer's submission regarding the need to monitor and adjust the doses of warfarin. Sections 4.4 and 5.1 of the Xarelto 20mg SPC stated that there was no need for the monitoring of coagulation parameters during treatment with rivaroxaban in clinical routine. However, if clinically indicated, rivaroxaban levels could be measured by certain tests. Section 4.4 of the SPC stated that 'Clinical surveillance in line with anticoagulation practice is recommended throughout the treatment period'. The Panel noted the recommended dose of Xarelto in the prevention of stroke and systemic embolism in patients with AF and certain risk factors was 20mg per day. Therapy was to be continued long-term

provided the benefit of prevention of stroke and systemic embolism outweighed the risk of bleeding. Dose adjustment was needed in patients with renal impairment.

The Panel did not consider there was a general claim that Xarelto was simple to use as alleged. 'Simple' was used to describe the dosing regimen. The dosing regimen for Xarelto was not as complicated as for other products in this therapeutic area and in this context the broad indication of one tablet once a day for a number of patient populations might be viewed as simple.

The Panel did not consider that the claim 'one tablet, once daily, simple' was inconsistent with the SPC and thus ruled no breach of Clause 3.2. Nor was the claim an inaccurate reflection of the risks of using anticoagulants as alleged. No breach of Clauses 7.2 and 7.9 was ruled.

Given its rulings above the Panel did not consider the company had failed to maintain high standards nor had it brought discredit to or reduced confidence in the pharmaceutical industry. No breach of Clauses 9.1 and 2 was ruled.

Complaint received **29 October 2012**

Case completed **28 November 2012**

ANONYMOUS v ELI LILLY and BOEHRINGER INGELHEIM

Promotional meeting allegedly disguised as education

A non-contactable clinician complained anonymously about a meeting held jointly by Lilly and Boehringer Ingelheim. The companies jointly marketed Trajenta (linagliptin), a dipeptidyl peptidase 4 (DPP-4) inhibitor for the management of type 2 diabetes and Jentadueto (linagliptin and metformin) also for the management of type 2 diabetes. Lilly also marketed Byetta (exenatide), a glucagon-like peptide-1 (GLP-1) receptor agonist for the management of types 1 and 2 diabetes.

The complainant stated that some years ago he/she had stopped meeting representatives because of their behaviour and the swollen numbers who sold the same medicine.

The complainant stated that Lilly's meeting was advertised as a means of understanding how the new diabetes medicines fitted into patient care. As a lead on diabetes the complainant thought this would be useful and probably in keeping with the meetings other companies had offered locally. However, despite the assurance of genuine medical education, the meeting overtly promoted Trajenta and Byetta. The speakers were little other than paid sales people for Lilly and the questionnaire asked which particular DPP-4 inhibitor the reader currently used and if the meeting had changed that choice. The complainant submitted that this clearly indicated that this was a sales meeting disguised as genuine education. As the meeting ended, the representatives poured into the meeting room and handed out prescribing information. The complainant understood that this was illegal.

The detailed responses from Lilly and Boehringer Ingelheim are given below.

The Panel noted that the complainant was anonymous and non-contactable. Such complaints were accepted and like all complaints judged on the evidence provided by the parties. The complainant had the burden of proving his/her complaint on the balance of probabilities.

The Panel did not know how the complainant had found out about the meeting. A journal advertisement which promoted the meeting was entitled 'Complexity of type 2 diabetes. A hands-on guide to simplify care in clinical practice'. A prominent highlighted box featured the sponsoring companies' logos and the explanation that 'These meetings have been developed by [the publisher of a diabetes journal] in conjunction with, and sponsored by, Boehringer Ingelheim Ltd and Eli Lilly and Company Limited'. In a separate highlighted box to the right were the logos for the journal and its publisher. Beneath the two boxes, in a prominent white typeface, the reader was told where to find prescribing information for linagliptin. The advertisement gave brief details of the programme committee and a short introduction alongside their photographs stated 'We have designed this series of complimentary meetings …' and 'We look forward to welcoming you …' although it was unclear who 'we' were. The invitation detailed the agenda for the half-day meeting which began at 12 noon with lunch and registration. Three presentations, 'All change! What you need to know about diagnosing type 2 diabetes now', 'Understanding the spectrum of different glucose-lowering drugs available', 'Understanding the relationship between diabetes, glucose-lowering drugs and cardiovascular disease' and 'Requirements after prescribing: what to monitor, when and why?' were followed by an 'Ask the experts session'. The meeting concluded at 4:45pm. The other invitation formats were closely similar in content although the layout differed; an email invitation provided a less detailed account of the agenda. All featured the prominent description of the companies' involvement and, all apart from a flyer, had a link to prescribing information. The Panel was concerned that the flyer did not contain prescribing information. All material had to be capable of standing alone in relation to Code compliance. There was no allegation in relation to the absence of prescribing information. The Panel noted that the prominent highlighted box describing the companies' involvement as 'in conjunction with, and sponsored by' appeared on pages 1, 2 and 4 of the four page flyer. The Panel considered it would have been helpful if more information about the status of the programme committee had been given and in that regard had some sympathy with the complainant. However, overall, the Panel considered that from the description of the companies' involvement, 'in conjunction with, and sponsored by', it was sufficiently clear that they did not have an arm's length arrangement with the publisher and that the companies' involvement went beyond the provision of finance. The average invitee would reasonably expect the agenda to discuss, *inter alia*, the companies' products and thus be categorized under the Code as promotional in this regard.

The Panel noted that it was also possible that the complainant had been invited by postal invitation or telephone. There was no way of knowing whether this was so and precisely what had transpired. The Panel noted that whilst representatives had delivered invitations, the complainant had stated that he/she had stopped meeting representatives some years ago.

The Panel noted that all meetings had to comply, *inter alia*, with the Code and have a clear educational content. The Panel noted that each presentation was accompanied by speaker notes.

The Chair's introductory presentation discussed the complexity of the current prescribing environment including cost. The first presentation discussed diagnosis including detailed case scenarios. The second presentation 'Understanding the spectrum of different glucose-lowering drugs available' outlined the advantages and disadvantages and discussed each class of medicine; linagliptin and exenatide were referred to. The presentation concluded with a discussion of published guidance on the management of hyperglycaemia (NICE, QUIPP etc); one of the take-home messages was 'However, the choice of agent depends on the specific circumstances and needs of the person with type 2 diabetes'. The third presentation, which discussed the relationship between diabetes, glucose-lowering drugs and cardiovascular (CV) disease, summarized CV outcomes of the major clinical trials. Cardiovascular outcome data for *inter alia*, exenatide and linagliptin were discussed. The final presentation discussed renal function monitoring and referred to medicines across all classes in relation to renal impairment. One slide favourably compared the clinical characteristics (dose adjustment, monitoring etc) of linagliptin with other DPP-4 inhibitors.

The Panel noted that speakers were briefed that, in addition to examining the key complexities of type 2 diabetes in clinical practice, the meetings aimed to provide information on the role of linagliptin and specifically in potentially reducing the management complexity of this condition. The Panel considered that such an aim was not necessarily unacceptable so long as the meetings and advertisements about them complied with the Code. The Panel noted its comments above about the impression given by the invitation. The Panel also noted that the detailed speakers' briefing in relation to the individual presentations appeared balanced and only mentioned linagliptin once.

The Panel noted the clear educational content of the meeting as set out above and ruled no breach of the Code. The Panel noted its comments above about the role of the companies, the publisher and the programme committee as set out in the invitations. The requirement in the Code about declarations and meetings related solely to sponsorship and in that regard the Panel considered that the companies' sponsorship had been disclosed on the invitations and on the slides; no breach of the Code was ruled.

It was not necessarily unacceptable for a questionnaire to enquire about a delegate's current and future prescribing decisions so long as it complied with the Code. Delegates did not have to provide the information. The Panel also noted that contrary to the complainant's account, the companies submitted that no representatives had entered the meeting room. It was not possible to determine where the truth lay. Whilst the parties' accounts differed, the Panel noted that it was not necessarily unacceptable for representatives to enter the main meeting room in relation to the meeting at issue.

The Panel noted that it had no way of knowing what was actually said by the speakers at the meeting in question. The Panel considered that the meeting was promotional for the companies' products mentioned. However, bearing in mind the impression given by the invitations as outlined above the Panel did not consider that its promotional nature was disguised as alleged; no breach of the Code was ruled. The Panel also ruled no breach of the Code in relation to maintenance of high standards.

A non-contactable clinician complained anonymously about a meeting held by Eli Lilly and Company Limited. Lilly stated in its response that, together with Boehringer Ingelheim Ltd, it had formed the Diabetes Alliance (the Alliance) and that the meeting in question was a joint meeting with Boehringer Ingelheim. The complaint was thus also taken up with that company (Case AUTH/2545/11/12).

Lilly and Boehringer Ingelheim jointly marketed Trajenta (linagliptin), a dipeptidyl peptidase 4 (DPP-4) inhibitor for the management of type 2 diabetes and Jentadueto (linagliptin and metformin) also for the management of type 2 diabetes. Lilly also marketed Byetta (exenatide), a glucagon-like peptide-1 (GLP-1) receptor agonist for the management of types 1 and 2 diabetes.

COMPLAINT

The complainant stated that some years ago he/she had stopped meeting pharmaceutical industry representatives because of the appalling record they had in terms of their behaviour in the promotion of their products as well as the swollen numbers of representatives who sold the same medicine.

In recent months the complainant had been led to believe that sharp practice was a thing of the past and that the companies were now more supportive of the NHS. Certainly some of them had helped the complainant's primary care trust (PCT) and provided good support for some meetings. The complainant had started to believe the leopard had changed its spots. Sadly this had been proved wrong.

The complainant stated that he/she had attended what was advertised as a genuine medical education event that turned into the bad old days of the pharmaceutical companies. Lilly's meeting, at a local hotel, was advertised as a means of understanding how the new medicines in diabetes fitted into patient care. As the complainant led on diabetes he/she thought this would be useful and probably in keeping with the meetings other companies had offered locally.

The complainant alleged that despite the assurance of genuine medical education, the meeting overtly promoted Trajenta and Byetta. The speakers were little other than paid sales people for Lilly. In fact, the questionnaire distributed asked, for example, which particular DPP-4 inhibitor the reader currently used and if the meeting had changed that choice.

The complainant submitted that this was a clear indication that this was a sales meeting disguised as genuine education. As the meeting came to an end, the representatives poured around the attendees into the meeting room and handed out prescribing information to take away. The complainant understood that this was illegal. The complainant stated that many of his/her colleagues were appalled.

The complainant stated that he/she and his/her colleagues considered that Lilly had set the industry back by years.

When writing to Lilly and Boehringer Ingelheim, the Authority asked the companies to respond in relation to Clauses 9.1, 12.1, 19.1 and 19.3 of the Code.

Case AUTH/2540/11/12

RESPONSE

Lilly submitted that the meeting in question was held in the 4 star Hilton Hotel in Blackpool on 7 November 2012. It was one of a series of identical promotional meetings entitled 'Complexity of type 2 diabetes, a hands-on guide to simplifying care in clinical practice', run at various venues throughout the UK. The meetings contained a certain amount of educational content as well as information on Trajenta. All materials relating to these meetings had been certified. The meetings were organised on the Alliance's behalf by a publishing group.

This series of promotional meetings was advertised via a number of channels:

- a meeting page in the events section of the website 'Diabetes on The Net'
- an advertisement in Diabetes in Practice, Diabetes Digest, Diabetes & Primary Care, Journal of Diabetes Nursing, The Diabetes Foot Journal, PCDS, Diabetes Care for Children & Young People
- a general email mailing
- a flyer accompanied by a meeting invitation sent by post or separately delivered by a representative during a promotional call.

It was not clear from the complaint which of these channels the complainant had responded to about the meeting. All items fulfilled the requirements for promotional materials including the product name, non-proprietary name, black triangle and prescribing information.

Trajenta and Jentadueto were currently the only licensed and marketed products of the Alliance. Although the meetings were promotional, it was clear from the agenda and the content of the presentations that the meetings were mainly educational, focusing on the overall management of type 2 diabetes. Lilly acknowledged that the meeting was promotional with respect to Trajenta, however, it strongly refuted the complainant's comments about the alleged promotion of Byetta. Whilst all classes of the medicines used to manage type 2 diabetes were discussed as per the agenda, a single mention of exenatide specifically was made on one slide with no use of the brand name; additionally exenatide was also mentioned along with other therapies in four other slides. All presentations in which any products were mentioned also ended by another clear slide informing the audience of the availability of prescribing information for Trajenta, in compliance with the Code.

Attendees were invited to arrive at the meeting from noon onwards. During registration they were advised that a buffet lunch was provided in a separate room, where a Trajenta promotional stand was set up and manned by three sales representatives from both companies. Copies of the materials used and displayed on the stand were provided. These included Trajenta and Jentadueto leavepieces, a quick reference guide to type 2 diabetes and chronic kidney disease and the Trajenta summary of product characteristics (SPC).

At about 12:45pm, delegates were asked to take their seats in a separate meeting room for the start of the presentations at 12:50pm. There was a half hour coffee break at 2:20pm and the meeting concluded with an 'Ask the experts' question and answer session. All delegates were given an evaluation form with the Trajenta prescribing information attached, a Continuing Professional Development Workbook and a programme book with speaker biographies. The agency staff collected any completed evaluation forms and handed out certificates of attendance. Lilly submitted that the Alliance representatives did not enter the meeting room either during or after the sessions. The representatives' interactions with delegates were limited to the room where the Trajenta stand was set up. Excluding Alliance staff, there were 26 attendees. Therefore, based on this, Lilly refuted the complainant's allegations.

The speakers were a head of a diabetes and endocrinology hospital department, a consultant diabetologist and a diabetes specialist nurse and nurse consultant. They were contracted and paid in accordance to the Alliance's procedures and policies on payments speaker contracts. They were invited and briefed by the agency.

Lilly submitted that all reasonable steps had been taken to ensure not only the transparency around the promotional nature of this meeting but also the high quality of the presentations. However, upon receiving this anonymous complaint, and in order to negate any possible misinterpretations for the remaining meetings of the series, it had contacted each registered attendee for upcoming meetings to remind them that Trajenta information would be discussed at the meeting and reiterated the option for them to unsubscribe from the meeting if they wish.

Based on the actions set out above, Lilly submitted that it had maintained high standards pre-meeting according to the Clause 9.1 and had provided clear information on the meeting in accordance with Clauses 12.1, 19.1 and 19.3 of the Code.

Case AUTH/2545/11/12

RESPONSE

Boehringer Ingelheim stated that it was fully aligned with Lilly's response.

Cases AUTH/2540/11/12 and AUTH/2545/11/12

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. Such complaints were accepted and like all complaints judged on the evidence provided by the parties. The complainant had the burden of proving his/her complaint on the balance of probabilities.

The complainant alleged that despite an assurance of genuine medical education the meeting overtly promoted Trajenta and Byetta. In this regard the complainant referred to the speakers, the questionnaire and commented on the conduct of representatives.

The Panel did not know how the complainant had found out about the meeting and it was not possible to contact the complainant to ascertain this. The journal advertisement which promoted the meeting was entitled 'Complexity of type 2 diabetes. A hands-on guide to simplify care in clinical practice'. A prominent highlighted box featured the sponsoring companies' names in logo format and the explanation that 'These meetings have been developed by [the publisher of a diabetes journal], in conjunction with, and sponsored by, Boehringer Ingelheim Ltd and Eli Lilly and Company Limited'. In a separate highlighted box to the right were the logos for the journal and publisher. Beneath the two boxes, in a prominent white typeface, the reader was told where to find prescribing information for linagliptin. The advertisement gave brief details of the programme committee and alongside their photographs gave a short introduction to the meeting. The introduction stated 'We have designed this series of complimentary meetings …' and 'We look forward to welcoming you …' although it was unclear who 'we' were. The invitation also detailed the agenda for the half-day meeting which began at 12 noon with lunch and registration. The Chair's address was followed by three presentations: 'All change! What you need to know about diagnosing type 2 diabetes now'; 'Understanding the spectrum of different glucose-lowering drugs available'; 'Understanding the relationship between diabetes, glucose-lowering drugs and cardiovascular disease' and 'Requirements after prescribing: what to monitor, when and why?'. The presentations were followed by an 'Ask the experts session'. The meeting concluded at 4:45pm. The other invitation formats were closely similar in content to the journal advertisement although the layout differed; the email invitation provided a less detailed account of the agenda. All featured the prominent description of the companies' involvement and, all apart from the flyer, had a link to prescribing information. The Panel was concerned that the flyer did not contain prescribing information. All material had to be capable of standing alone in relation to Code compliance. There was no allegation in relation to Clause 4.1 and prescribing information. The Panel noted that the prominent highlighted box describing the companies' involvement as 'in conjunction with, and sponsored by' appeared on pages 1, 2 and 4 of the four page flyer. The Panel considered it would have been helpful if more information about the status of the programme committee had been given and in that regard had some sympathy with the complainant. However, overall, the Panel considered that the description of the companies' involvement as 'in conjunction with, and sponsored by' made it sufficiently clear that the companies did not have an arm's length arrangement with the publisher and that the companies' involvement went beyond the provision of finance. The average invitee would reasonably expect the agenda to discuss, *inter alia*, the companies' products and thus be categorized under the Code as promotional in this regard.

The Panel noted that it was also possible that the complainant had been invited by postal invitation or telephone. There was no way of knowing whether this was so and precisely what had transpired. The Panel noted that whilst representatives had delivered invitations, the complainant had stated that he/she had stopped meeting representatives some years ago.

The Panel noted that all meetings had to comply, *inter alia*, with Clause 19 of the Code and have a clear educational content. The Panel noted that each presentation was accompanied by speaker notes. The Chair's introductory presentation discussed the complexity of the current prescribing environment including cost. The first presentation discussed diagnosis including detailed case scenarios. The second presentation 'Understanding the spectrum of different glucose-lowering drugs available' outlined the advantages and disadvantages and discussed each class of medicine. Pioglitazone was discussed and within the DPP-4 section linagliptin, saxagliptin, sitagliptin and vildagliptin. Two slides compared linagliptin with glimepiride in relation to their effect on HbA1c and weight change. Exenatide and insulin detemir were discussed in relation to GLP-1 receptor agonists and insulin in combination. The presentation concluded with a discussion of published guidance on the management of hyperglycaemia (NICE, QUIPP etc) and concluded with a take-home message slide which featured the statement 'However, the choice of agent depends on the specific circumstances and needs of the person with type 2 diabetes'. The third presentation, which discussed the relationship between diabetes, glucose-lowering drugs and cardiovascular (CV) disease, summarized CV outcomes of the major clinical trials. It featured a trial which compared the glucose-lowering efficacy and risk of CV events of certain sulphonylureas. Cardiovascular outcome data for liraglutide, saxagliptin and exenatide and linagliptin were discussed. The last section briefly summarized CV data for certain older glucose-lowering therapies including pioglitazone and insulin glargine. The final presentation discussed

monitoring and reviewing diabetics and their therapies and referred to medicines across all classes in relation to renal impairment. One slide favourably compared the clinical characteristics (dose adjustment, monitoring etc) of linagliptin with other DPP-4 inhibitors.

The Panel noted that the introduction to the speakers' briefing document stated that in addition to examining the key complexities of type 2 diabetes in clinical practice, the meetings aimed to provide information on the role of linagliptin and specifically in potentially reducing the management complexity of this condition. The Panel considered that such an aim was not necessarily unacceptable so long as the meetings and advertisements about them complied with the Code. The Panel noted its comments above about the impression given by the invitation. The Panel also noted that the detailed speakers' briefing in relation to the individual presentations appeared balanced and only mentioned linagliptin once.

The Panel noted the clear educational content of the meeting as set out above and ruled no breach of Clause 19.1. The Panel noted its comments above about the role of the companies, the publisher and the programme committee as set out in the invitations. Clause 19.3 related solely to sponsorship and in that regard the Panel considered that the companies' sponsorship had been disclosed on the invitations and on the slides; no breach of Clause 19.3 was ruled.

It was not necessarily unacceptable for a questionnaire to enquire about a delegate's current and future prescribing decisions so long as it complied with the Code. Delegates did not have to provide the information. The Panel also noted that contrary to the complainant's account, the companies submitted that no representatives had entered the meeting room. It was not possible to determine where the truth lay. Whilst the parties' accounts differed, the Panel noted that it was not necessarily unacceptable for representatives to enter the main meeting room in relation to the meeting at issue.

The Panel noted that it had no way of knowing what was actually said by the speakers at the meeting in question. The Panel considered that the meeting was promotional for the companies' products mentioned. However, bearing in mind the impression given by the invitations as outlined above the Panel did not consider that its promotional nature was disguised as alleged; no breach of Clause 12.1 was ruled.

Noting its rulings above, the Panel ruled no breach of Clause 9.1.

During its consideration of this case the Panel noted that invitees were advised that the meetings were sponsored jointly by Lilly and Boehringer Ingelheim and their promotional scope was thus not limited to products promoted by the Alliance. The Panel considered that the prescribing information for Byetta or a relevant link thereto ought to have been included on all materials. In addition prescribing information for Jentadueto ought not to have been limited to the presentations but should have appeared on the invitations. There was no allegation on these points. The Panel requested that the companies be advised of its view.

Complaint received **13 November 2012**

Case completed **20 December 2012**

CODE OF PRACTICE REVIEW – February 2013

Cases in which a breach of the Code was ruled are indexed in **bold type.**

2411/6/11	**Pharmacosmos v Vifor**	**Ferinject video**	**Breaches Clauses 4.1 and 4.3. Two breaches Clause 7.2** **Audit and two re-audits required by Appeal Board.** **Recovery of video required by Appeal Board.**	**Report from Panel to Appeal Board.**	**Page 3**
2422/7/11	**Pharmacosmos v Vifor**	**Ferinject leavepiece**	**Two breaches Clause 7.2** **Audit and two re-audits required by Appeal Board.**	**Report from Panel to Appeal Board.**	**Page 10**
2435/6/12	**GlaxoSmithKline/ Director v Chiesi**	**Promotion of an unlicensed indication and breach of undertaking**	**Breaches Clauses 1.8, 2 and 3.2** **Two breaches Clause 9.1** **Two breaches Clause 25** **Audit and re-audit required by Appeal Board.** **Public reprimand required by Appeal Board.**	**Report from Panel to Appeal Board.**	**Page 15**
2509/6/12	**Anonymous/ Roche**	**Conduct of employees**	**Breach Clause 9.1**	**Appeal by respondent**	**Page 25**
2515/6/12	Allergan/Director v Merz	Alleged breach of undertaking	No breach	Appeal by complainant	Page 33
2525/7/12	Clinical Lead Pharmacist v ProStrakan	Conduct of representatives	No breach	No appeal	Page 40
2527/8/12	Anonymous v Shire	Alleged promotion prior to grant of marketing authorization	No breach	No appeal	Page 44
2529/9/12	**Anonymous/ Director v Vifor**	**Breach of undertaking**	**Breaches Clauses 2, 9.1 and 25**	**No appeal**	**Page 53**
2531/9/12	Consultant in Palliative Medicine v ProStrakan	Conduct of representative	No breach	No appeal	Page 56
2533/10/12	**Anonymous v Bayer**	**Representative call rates**	**Breaches Clauses 9.1 and 15.9**	**No appeal**	**Page 58**
2534/10/12	Anonymous v Roche	Alleged inducement to continue with project	No breach	No appeal	Page 63
2537/10/12	Anonymous v Bayer	Promotion of Xarelto	No breach	No appeal	Page 65
2540/11/12 & 2545/11/12	Anonymous v Lilly and Boehringer Ingelheim	Promotional meeting allegedly disguised as education	No breach	No appeal	Page 69

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 administrative staff 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 detail aids and other printed or electronic material used by representatives
- the supply of samples
- the provision of 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 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
- 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 and donations 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
facsimile 020 7747 8881
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