NUMBER 81 August 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.

ANNUAL REPORT FOR 2012

The Annual Report of the Prescription Medicines Code of Practice Authority for 2012 will be published on our website (www.pmcpa.org.uk) shortly and copies will be sent to all who are on the mailing list for the Code of Practice Review.

There were 78 complaints in 2012 compared with 84 complaints in 2011. There were 86 complaints in 2010.

The 78 complaints in 2012 gave rise to 84 cases. The number of cases usually differs from the number of complaints, the reason being that some complaints involve more than one respondent company and some complaints do not become cases at all because they are withdrawn.

Of the 296 rulings made by the Code of Practice Panel in 2012, 253 (85%) were accepted by the parties, 31 (11%) were unsuccessfully appealed and 12 (4%) were successfully appealed. This compares with the 8% of rulings which were successfully appealed in 2011.

As is usually the case, the number of complaints made by health professionals in 2012 exceeded the number made by pharmaceutical companies, there being 21 from health professionals and 16 from pharmaceutical companies.

The average time to deal with all cases in 2012 was 11.6 weeks (8.8 weeks in 2011). There was an increase in the time taken for cases settled at the Panel level, 9.9 weeks in 2012 (7 weeks in 2011) and cases which were appealed, 18.9 weeks in 2012 (15 weeks in 2011).

Each quarter the Authority advertises brief details of cases completed in the previous three months where companies were ruled in breach of Clause 2 of the Code, were required to issue a corrective statement or were the subject of a public reprimand. These advertisements which are published on the PMCPA website and placed in the BMJ, The Pharmaceutical Journal and the Nursing Standard act as a sanction and highlight what constitutes a serious breach of the Code.

PHARMACEUTICAL REPRESENTATIVE VISIT REQUEST FORMS

The Authority has recently received examples of pharmaceutical representative visit request forms issued by various medicines management teams. The purpose of such forms is for the representatives to provide the teams with a brief outline of what they want to talk to them about. Although the precise detail of the forms differs slightly, the information typically requested consists of the representative's name, contact details etc, name of the medicine, its indication and the reason for the visit. The medicines management teams use the information provided to decide whether they want to see the representative; if they do they can then make the most of the appointment by knowing in advance what topics are to be discussed. The Authority accepts that the forms may be a valuable tool to help medicines management teams make the best use of their resources but is concerned that, in complying with a request to complete one of the forms, representatives are unwittingly creating a piece of promotional material which is unlikely to comply with the Code.

Continued overleaf...

PROPOSALS TO AMEND THE ABPI CODE OF PRACTICE FOR THE PHARMACEUTICAL INDUSTRY AND THE PMCPA CONSTITUTION AND PROCEDURE HAVE BEEN SENT TO COMPANIES AND PUBLISHED ON THE PMCPA WEBSITE

The proposed amendments result from the new EFPIA Code on Disclosure of Transfers of Value from Pharmaceutical Companies to Healthcare Professionals and Healthcare Organisations and changes to the EFPIA Code on the Promotion of Prescription-Only Medicines to, and Interactions with, Healthcare Professionals. Other proposals to amend the ABPI Code and the PMCPA Constitution and Procedure are also included.

The proposals have been sent to the Medicines and Healthcare Products Regulatory Agency (MHRA), the British Medical Association (BMA), the Royal Pharmaceutical Society (RPS) and the Royal College of Nursing (RCN) as required by the Constitution and Procedure. They have also been sent to the Serious Fraud Office (SFO).

The proposals are the subject of public consultation and comments must be submitted to hsimmonds@pmcpa.org.uk as soon as possible and by no later than Thursday, 5 September.

All the relevant documents concerning the consultation are available on the PMCPA website

Continued overleaf...

CODE OF PRACTICE TRAINING

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

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

The next Code of Practice seminar date on which places remain available is:

Friday, 27 September

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

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

HOW TO CONTACT THE AUTHORITY

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

www.pmcpa.org.uk

Telephone: 020 7747 8880
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
Tannyth Cox: 020 7747 8883

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

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

PROPOSALS TO AMEND THE ABPI CODE OF PRACTICE... (Continued from cover)

(www.pmcpa.org.uk). To set the proposals in context a draft copy of the 2014 Code has also been made available. This draft will be subject to further changes.

It is anticipated that final proposals will be agreed by the ABPI Board of Management in October and then come before the ABPI Half Yearly General Meeting on Tuesday, 5 November with a view to approval by member companies. If approved, the new Code of Practice would come into effect on 1 January 2014 with a transition period of four months.

SUBCONTRACTORS AND THE CODE

The Authority has considered cases recently whereby a third party engaged by a pharmaceutical company engaged a subcontractor to do some of the work in question. The subcontractor in turn engaged a further subcontractor to do some additional work on the project. Companies must be alert to this possibility and ensure that their policies and procedures address potential subcontracting. Companies will be held responsible under the Code for all third parties which undertake work on their behalf whether engaged directly or indirectly. In that regard Clause 16.1 requires all relevant personnel including third parties to be fully conversant with the Code.

PHARMACEUTICAL REPRESENTATIVE VISIT REQUEST FORMS (Continued from cover)

The aim of the Code is to ensure that the promotion of medicines to health professionals and to administrative staff is carried out within a robust framework to support high quality patient care. No promotional material should be issued unless its final form, to which no subsequent amendments will be made, has been certified by two persons on behalf of the company. Given the logistical problems in separately certifying pharmaceutical representative visit request forms from every medicines management team to ensure that the completed forms comply with the Code, the Authority suggests that companies consider pre-approving material which will provide the medicines management teams with the brief overview that they need and ensure that the representatives do not create their own pieces of promotional material. It would be helpful if, on such material, it is explained to the medicines management teams why their forms cannot be completed by the representative.

EX-EMPLOYEE v ASTRAZENECA

Promotion of Seroquel

An ex-employee of AstraZeneca complained about the promotion of Seroquel (quetiapine) by that company and referred to five presentations, dated 1999, 2001, 2002, 2004 and 2006 respectively, published in the archived material for investors section of the company's website (AstraZeneca.com). The presentations had, three months earlier, been the subject of an alleged breach of undertaking, Case AUTH/2538/10/12.

The complainant noted that in Case AUTH/2538/10/12, AstraZeneca had stated in a letter to the PMCPA that 'It is also clear from the chronology of the presentations that AstraZeneca's statements in relation to weight and Seroquel evolved as a balanced and fair reflection of the evidence available at the time'. The complainant contended that this was not the case and noted a CBS news article entitled 'Email: AstraZeneca knew in 1997 that Seroquel caused weight gain'.

The complainant stated that the presentations demonstrated how AstraZeneca spread false claims about Seroquel and its effect on body weight.

The complainant explained that he was responsible for sign off for Seroquel in the UK and in 1997-9 the evidence clearly showed Seroquel caused weight gain. This was both time and dose dependent. Consequently, the complainant was unwilling to sign off any weight claims for UK advertisements.

In support of his position the complainant referred to the blog of a retired US psychiatrist and cited ten internet links.

The detailed response from AstraZeneca is given below.

The Panel did not accept AstraZeneca's assertion that a statement made in its response to Case AUTH/2538/10/12 was outside the scope of the Code. The complaint to be considered was about AstraZeneca's statements in relation to weight and Seroquel in the five presentations and whether these were a balanced and fair reflection of the evidence available at the time.

The Panel noted that the complainant had not highlighted specific slides. In Case AUTH/2538/10/12 the Panel had identified eight slides in the presentations at issue which contained claims about Seroquel and weight in relation to the alleged breach of the undertaking given in Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10. It was the Authority's responsibility to ensure compliance with undertakings. The Panel noted that the circumstances of the present case, Case AUTH/2572/1/13, were different. The Panel noted that the complainant made a general allegation but had not submitted any detailed reasons. Blog postings about Seroquel and AstraZeneca provided by the complainant largely concerned commentary on internal company documents disclosed during US litigation. The complainant did not explain how or which part of these supported the allegation. Whilst some of the blog postings discussed, *inter alia*, general issues about Seroquel and weight there was no mention of the claims identified in the eight slides considered in Case AUTH/2538/10/12 and nor was there detailed discussion of the clinical data. The complainant had not alleged that the claims were in breach of the Code for the reasons set out in Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10 ie that the presentations stated or implied that Seroquel was the only atypical antipsychotic with a favourable weight profile or that it had a clear advantage in this regard.

The Panel was concerned that AstraZeneca had not responded to the substantive allegation that the presentations were not a fair and balanced reflection of the evidence available at that time. The Panel noted the company's submission that any response would be no more than a reiteration of its submission in Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10 in which a breach of the Code was ruled. The Panel noted its general comments above in this regard. In particular, the Panel noted that the statements about Seroquel and weight in the presentations at issue did not state or imply that Seroquel was the only atypical antipsychotic with a favourable weight profile and were thus different to the material previously considered.

It was not the Panel's role to infer detailed reasons to support a complainant's allegation. It was for the complainant to establish his case on the balance of probabilities. The Panel considered that the very general nature of the complaint was such the complainant had not discharged his burden of proof and the Panel, on this narrow ground, ruled no breach of the Code. This ruling was appealed by the complainant.

Upon appeal by the complainant, the Appeal Board noted that in Case AUTH/2538/10/12 the complainant had unsuccessfully alleged that the five presentations at issue, dated 1999, 2001, 2002, 2004 and 2006 respectively, were in breach of the undertaking given in Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10. (These cases concerned a Seroquel journal advertisement published in April 2004 which included an implied claim of no weight gain; breaches of the Code were ruled).

The Appeal Board noted that alleged breaches of undertaking were taken up with the Director nominally acting as the complainant as the

PMCPA was responsible for ensuring compliance with undertakings. The current case (Case AUTH/2572/1/13), however, was different as it concerned an alleged breach of the Code in which the Panel made its rulings based on the parties' submissions. The burden was on the complainant to show, on the balance of probabilities, that a breach of the Code had occurred. Neither the Panel nor the Appeal Board were investigative bodies. In that regard the Appeal Board was concerned that the complainant had not clearly identified the claims at issue and, in relation to each, set out a concise explanation and discussion of the data to support his allegation.

The Appeal Board was concerned that the nature of the material before it was such that it was not always clear how/whether the material supported the complainant's allegation. Extracts from emails and excerpts from published papers were provided. The context of such material was unclear. The Appeal Board had to decide how much weight to attach to this evidence.

The Appeal Board noted that the Seroquel summary of product characteristics (SPC) dated 19 April 1999 stated in Section 4.8 Undesirable Effects, that 'As with other antipsychotics, Seroquel may also be associated with limited weight gain, predominantly during the early weeks of treatment.' A closely similar statement was included in the August 2002 SPC. By November 2006 'limited' had been removed and the statement now read 'As with other antipsychotics, Seroquel may be associated with weight gain, predominantly in the early weeks of treatment.'

The Appeal Board noted that the claims about weight in the presentations at issue were as follows: 'Seroquel - minimal weight gain' (1999); 'weight neutral in the long term' (2001); 'Weight-neutral long-term' and 'weight-neutral in the long term' (2002); 'Favourable weight profile long-term' (2004); 'Less weight gain than with olanzapine' (2006). The Appeal Board noted that the complainant considered that the latter comparative claim was truthful.

The Appeal Board considered that there was insufficient evidence provided by the complainant to show that the presentations, when written, did not provide a fair and balanced reflection of the evidence available at the time regarding weight gain with Seroquel. The Appeal Board considered that the complainant had not discharged his burden of proof and it upheld the Panel's ruling of no breach of the Code. The appeal was unsuccessful.

An ex-employee of AstraZeneca UK Limited complained about the promotion of Seroquel (quetiapine) by that company and referred to five presentations which three months earlier had been the subject of an alleged breach of undertaking, Case AUTH/2538/10/12. During the consideration of that case, and in response to a query from the complainant, he was advised that although the presentations had been ruled not to be in breach of Clause 25, he could, under the Constitution and Procedure, make a separate complaint about their content. After submitting the present complaint (Case AUTH/2572/1/13) and after AstraZeneca had been asked to respond to it, the complainant clarified that the present complaint did not concern an alleged breach of undertaking. The complainant was asked to provide further and better particulars clearly stating the material at issue and why it was considered to be in breach of the Code. As stated in the introduction to the Constitution and Procedure, a complainant had the burden of proving their complaint on the balance of probabilities. The PMCPA's advice to all complainants was always to provide a clear and concise exposition of the facts. The case proceeded as an alleged breach of Clause 7.2 and AstraZeneca was asked to respond to the complaint.

The presentations at issue, which had been published in the archived material for investors section of the company's website (AstraZeneca.com), were dated 1999, 2001, 2002, 2004 and 2006 respectively.

COMPLAINT

The complainant was concerned about a number of presentations produced by AstraZeneca. The complainant noted that in a letter to the PMCPA in connection with Case AUTH/2538/10/12, AstraZeneca stated 'It is also clear from the chronology of the presentations that AstraZeneca's statements in relation to weight and Seroquel evolved as a balanced and fair reflection of the evidence available at the time'. The complainant contended that this was not the case and noted a CBS news email article entitled 'Email: AstraZeneca knew in 1997 that Seroquel caused weight gain'.

The complainant stated that the presentations on AstraZeneca's website had allowed him to see how high up in the organisation people were involved in spreading false claims about Seroquel and its effect on body weight.

These presentations looked like poor quality detail aids that he would never have approved when he was at AstraZeneca UK.

AstraZeneca had submitted that 'AZ's statements in relation to weight and Seroquel evolved as a balanced and fair reflection of the evidence available at the time'. The complainant contended that this was not so.

The complainant was responsible for sign off for Seroquel in the UK and in 1997-9 the evidence clearly showed Seroquel caused weight gain that was both time and dose dependent. Consequently, the complainant was unwilling to sign off any weight claims for UK advertisements.

One of the best reports on what AstraZeneca got up to was available on the blog of a retired US psychiatrist. The complainant referred to ten blog articles on Seroquel.

The complainant was disappointed at being called a 'vexatious ex-employee' by AstraZeneca. The complainant worked with many good people at

AstraZeneca, but there were some who were not. Also there were some who stayed quiet who shouldn't have.

The Authority initially asked AstraZeneca to respond in relation to Clauses 2, 9.1 and 25. Subsequently AstraZeneca was asked to respond to Clause 7.2 of the Code.

RESPONSE

AstraZeneca queried whether this case should be allowed to proceed and raised three main concerns under the Constitution and Procedure; whether the case had been the subject of a previous adjudication; whether it was within the scope of the Code to raise an allegation about the accuracy of a statement made in a company's response; whether it was appropriate to ask the company to respond again to a complaint it had already responded to in full.

In AstraZeneca's view this complaint was very similar to Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10; although the specifics of the present claims differed from the 2010 cases the essence of the allegation was the same. Any AstraZeneca response in relation to Clause 7.2 would be no more than a reiteration of the argument it put forward in 2010 which was unsuccessful and resulted in a breach of, *inter alia*, Clause 7.2.

AstraZeneca noted that evidence submitted by the complainant comprised links to US news articles and blogs none of which had scientific foundation or offered new data relevant when the claims were made, nor were they relevant to the UK – thus no new evidence had been adduced. The company requested that the matter be reviewed by the Director; if the Director concluded that the complaint should be considered by the Panel the correspondence submitted in this request should be used as the full response to the complaint.

AstraZeneca was surprised that the PMCPA had advised the complainant that he could make a further complaint about the presentations and was astonished that the PMCPA did not dismiss the second complaint when it subsequently received the details.

AstraZeneca noted that the second complaint directly followed Case AUTH/2538/10/12, which also concerned the presentations. In that case, on four out of the five presentations at issue, the Panel ruled no breach of the Code. Instead of appealing those rulings (which would have been the proper course of action if the complainant disagreed with the Panel's conclusions), he brought a fresh complaint about the same presentations, apparently having received reassurance that this would be acceptable. From his short complaint, it did not transpire what violation of the Code was alleged. The complaint concerned the presentations, yet the complainant contended that the statement 'It is also clear from the chronology of the presentations that AstraZeneca's statements in relation to weight and Seroquel evolved as a balanced and fair reflection of the evidence available at the time' made in AstraZeneca's response to Case AUTH/2538/10/12, was incorrect. In objecting to this statement, the complainant referred to an article published in 2009 on the CBS news website with the headline 'E-Mail: AstraZeneca Knew in 1997 that Seroquel Caused Weight Gain'.

AstraZeneca contended that the Panel should have recognised that Case AUTH/2572/1/13 was an improper manipulation of the complaints procedure by an aggrieved ex-employee and thus dismissed it from the start: firstly because it was without substance (AstraZeneca was at a genuine loss to understand what it was required to respond to, which interfered with its right of defence) and secondly, because allowing the complaint to progress contravened the Constitution and Procedure. In relation to four out of the five presentations at stake, the matter had already been ruled upon and did not fall within the limited circumstances where the PMCPA had discretion to rule on a matter already adjudicated. With regard to the fifth presentation AstraZeneca noted that its appeal of the Panel's ruling in Case AUTH/2538/10/12 of breaches of Clauses 2, 9.1 and 25 was pending.

AstraZeneca alleged that by entertaining a complaint such as this, the PMCPA gave fuel to vexatious complainants to make absurd claims, resulting in a mockery of the system.

1 The complaint was without substance

AstraZeneca stated that it was at a genuine loss to understand what it was required to respond to. Whether the complaint was about the presentations or about the response letter, it was absurd on its face. AstraZeneca stated that it should not have to guess what the complainant had in mind.

<u>The presentations</u>

AstraZeneca submitted that this was apparently a complaint about the presentations. Indeed, in correspondence with the PMCPA the complainant stated: 'Thank you for your recent letter confirming that I can make a fresh complaint about the presentations listed below. I now do so'. Further, the PMCPA had treated the complaint as such. Although it did not transpire what violation of the Code the complainant alleged, AstraZeneca had been asked to respond to Clauses 2, 9.1 and 25, which meant that the PMCPA was treating this as a breach of undertaking case.

Effectively, therefore, the PMCPA had asked AstraZeneca to respond to the allegation that the presentations contained statements in breach of AstraZeneca's undertaking in Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10. AstraZeneca alleged that, however, this was precisely the issue on which the Panel had already ruled.

If the presentations were the subject of the complaint, then surely the Panel would agree that neither the statement quoted by the complainant in the response letter, nor the CBS news article, were relevant to the consideration of whether AstraZeneca had breached its undertaking.

The response letter

If, however, (and contrary to the PMCPA's explicit indications to the contrary, above), the subject of the complaint was, in fact, the response letter, then this too was absurd. The Panel surely agreed that the response letter, which formed part of the correspondence in relation to Case AUTH/2538/10/12, could not itself be the subject of a separate complaint under the Code. If this were possible, it would totally undermine the industry's right to defend itself.

In fact, a company's submission to the PMCPA would, very clearly, fall outside the Code. The Code applied to the promotion of medicines, as well as certain categories of non-promotional information (Clause 1.1); and the PMCPA's remit, according to the Constitution and Procedure, was limited to handling 'Complaints made under the Code about promotional material or the promotional activities of companies' (Introduction). Whilst in practice (and consistent with Clause 1.1) the PMCPA also handled complaints about non-promotional materials and activities in so far as these fell within the scope of the Code, a company's submission to the PMCPA in response to a complaint was not akin to these non-promotional categories of information, and could not be the subject of a complaint.

Further, in so far as the complainant objected to the response letter, he had had the opportunity to appeal the Panel's rulings of no breach of the Code but had not done so. In fact, even if the complainant had appealed, any objection to what AstraZeneca stated in the response letter would be relevant only in so far as that statement was material to the Panel's rulings. The statement made by AstraZeneca and quoted by the complainant (namely, 'It is also clear from the chronology of the presentations that AstraZeneca's statements in relation to weight and Seroquel evolved as a balanced and fair reflection of the evidence available at the time') was not material to the Panel's rulings. Indeed, it was very clear that the only issue the Panel considered in Case AUTH/2538/10/12 was whether AstraZeneca had breached its undertaking, and not whether the statements made in the presentations were balanced, fair and an accurate reflection of the evidence. This was why, for example, the Panel stated in its ruling regarding the one presentation ruled in breach of the Code that 'it was only considering whether or not there had been a breach of undertaking', not the accuracy of the claims. Consistent with this, it was important to emphasise that if the Panel had considered it relevant to comment on or take issue with the statement in the response letter that the complainant had objected to, it had the opportunity to do so in its ruling in Case AUTH/2538/10/12. However, rightly, it did not do so.

Further, and in any event, the statement in AstraZeneca's response letter, and referred to by the complainant, did not fall within the scope of the undertaking. As a consequence of the undertaking, AstraZeneca was not entitled to claim or imply that Seroquel was the only atypical with a favourable weight profile. Accordingly, by explaining to the PMCPA that AstraZeneca's statements in relation to weight and Seroquel evolved as a balanced and fair reflection of the evidence available at the time, AstraZeneca had not claimed or implied that Seroquel was the only atypical with a favourable weight profile. As explained above, the only issue for the Panel to consider in a breach of undertaking case was whether a claim made in material which fell within the scope of the Code was the same as or similar to one previously ruled in breach of the Code.

AstraZeneca submitted that accordingly, either the presentations were the subject matter of the complaint for breach of undertaking, which would be absurd because the Panel had ruled on precisely this issue in Case AUTH/2538/10/12, or its response letter was the subject matter of the complaint, which would be absurd because it did not constitute material which fell within the scope of the Code (being a submission made in the context of a complaint procedure). For the avoidance of any doubt, it was clear that the CBS news article was not itself the subject of the complaint. The present complaint (Case AUTH/2572/1/13) was thus without substance.

2 Contravention of the Constitution and Procedure

AstraZeneca contended that the complaint violated Paragraph 5.2 of the Constitution and Procedure which made clear that, where a complaint concerned a matter 'closely similar' to one which had been the subject of a previous adjudication, the circumstances in which it might be allowed to proceed were very limited. This case concerned a matter not just 'closely similar' to Case AUTH/2538/10/12, but actually identical, as explained above. Specifically, AstraZeneca was apparently asked to defend again an alleged breach of undertaking in relation to the presentations. In any event, not one of the three circumstances in which a second complaint was allowed to proceed applied here, as explained below.

- Firstly, no new evidence was adduced by the complainant. The complainant referred only to a statement made by AstraZeneca in the response letter and to the CBS news article. Neither constituted 'evidence' that, in maintaining the presentations on its website, AstraZeneca breached its undertaking. The presentations had to be assessed on their own terms in light of the undertaking. This was what the Panel did in its ruling in Case AUTH/2538/10/12, which was, in part, subject to an appeal. Further, for the sake of completeness, AstraZeneca noted that it made a similar statement in its response to Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10; and press articles/broadcasts which criticised AstraZeneca's alleged suppression of evidence regarding the effect of Seroquel on weight (ie very similar to the CBS news article) were also under discussion in those 2010 cases. The complainant had not adduced any new evidence of breach of the undertaking.
- Secondly, the passage of time did not raise doubt as to whether the same decision would be made in respect of this case. The ruling in Case AUTH/2538/10/12 was dated 3 January 2013 and this Case (Case AUTH/2572/1/13) followed 12 days later (it was received by the PMCPA on 15

January 2013).
- Thirdly, there had not been any change in circumstances which raised doubts as to whether the same decision would be made in respect of this case.

Allowing this complaint to proceed, therefore, contravened the Constitution and Procedure.

Further, the Panel's ruling was, in part, still subject to adjudication by the Appeal Board. Accordingly, if the PMCPA allowed this complaint to proceed, it not only contravened the Constitution and Procedure by re-opening a case where none of the three circumstances above applied, but also, re-started a case which was, in part, still pending consideration by the Appeal Board. This was highly irregular and prejudicial to AstraZeneca.

For the sake of completeness, the following wording in Paragraph 5.2 of the Constitution and Procedure (also quoted above) had no bearing on whether the present complaint should be allowed to proceed: 'The Director should normally allow a complaint to proceed if it covers matters similar to those in a decision of the Panel where no breach of the Code was ruled and which was not the subject of appeal to the Appeal Board'. Clearly, this wording was not intended to allow the same complainant to issue a fresh complaint as an alternative to appealing the Panel's ruling on the original complaint. Rather, the Constitution and Procedure must be interpreted as providing that a different complainant (who would not have recourse to appealing the original complaint, to which he/she was not a party), would be permitted, normally, to bring a fresh complaint in the event that the matter had not been the subject of an appeal. In this case, however, the complainant could have appealed the Panel's rulings of no breach of the Code in relation to four out of the five presentations at stake in Case AUTH/2538/10/12, had he so wished. Indeed, the advice on the PMCPA website regarding the complaints procedure under the heading 'Can the Panel's ruling be changed?' (dated 2 May 2012), clearly stated that:

'Once the Panel has completed its consideration of a case and informed the parties of the outcome, it has no further role to play in that case. The Panel ruling provides a complete account of the factors in the case that the Panel considered were important in making its ruling. There is no provision in the Constitution and Procedure for the Panel to comment on the reasoning set out in its ruling. Similarly there is no way for the Panel ruling to be changed.

If either party considers that the Panel has made the wrong ruling for whatever reason then their only recourse is to appeal.'

Further, and as explained above, the Panel's ruling in Case AUTH/2538/10/12 was, in part, under appeal.

Conclusion

AstraZeneca stated that the complainant's submission of a fresh complaint about the presentations, instead of appealing the Panel's rulings in Case AUTH/2538/10/12, was an improper attempt to put the same matter before the PMCPA. This kind of vexatious complaint should not be entertained.

Accordingly, AstraZeneca respectfully requested that, the case preparation manager dismiss this case and not place it before the Panel (Paragraph 5.1 of the Constitution and Procedure). Alternatively, AstraZeneca requested that the Director exercise power under Paragraph 5.2 of the Constitution and Procedure to decide that the complaint should not proceed on the basis that it did not satisfy the Paragraph 5.2 for 'similar' matter and/or that the present complaint did not show any breach of the Code.

AstraZeneca reiterated that it genuinely did not understand what it had to respond to. However, in the event that the PMCPA disagreed with the arguments raised above and had construed the complaint differently, AstraZeneca requested the opportunity of further response. Clearly, it would be unfair for this matter to proceed to a ruling when the allegation against AstraZeneca did not make any sense.

PANEL RULING

The Panel noted that the five presentations at issue dated 1999, 2001, 2002, 2004 and 2006 respectively had been the subject of a previous complaint by the same complainant (Case AUTH/2538/10/12) wherein it was alleged that they were in breach of an undertaking relating to Seroquel and claims about weight given in Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10. (These cases concerned a journal advertisement for Seroquel published in April 2004). In Case AUTH/2538/10/12, the Panel, and in relation to one presentation the Appeal Board ruled no breach of the Code. The complainant now queried whether these five presentations were a balanced and fair reflection of the evidence alleging that in 1997-1999 when the complainant was responsible for UK sign off for Seroquel it was clear that Seroquel caused weight gain. In support the complainant cited 10 blog postings authored by a retired psychiatrist in the US.

AstraZeneca had not submitted a comprehensive response to the present complaint which alleged a breach of Clause 7.2. In its response AstraZeneca referred to previous correspondence relating to this case including its response to the earlier correspondence with regard to a possible breach of Clause 25. The company submitted that the present complaint, ie the alleged breach of Clause 7.2, should not have been allowed to proceed and requested that this matter be placed before the Director for consideration. AstraZeneca had been asked by the case preparation manager to submit a response.

The Panel noted that the points raised by AstraZeneca were matters for consideration by the case preparation manager in accordance with the Constitution and Procedure. In particular, AstraZeneca's submission that the essence of the present allegation was the same as that in

Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10 and had therefore been the subject of a previous adjudication and in accordance with Paragraph 5.2 of the Constitution and Procedure should not proceed.

These 2010 cases concerned a Seroquel journal advertisement published in April 2004 (Cases AUTH/2294/1/10 and AUTH/2297/1/10) and an online news item (Case AUTH/2296/1/10) which referred to the advertisement at issue in Cases AUTH/2294/1/10 and AUTH/2297/1/10. In these cases, the Panel had noted that the material implied that Seroquel was the only one with 'a favourable weight profile across the full dose range'. Given that the other medicines caused weight gain, the advertisement could be read as implying that Seroquel did not. This was not so. Similarly, the advertisement could be read as implying that Seroquel had a clear advantage regarding its 'favourable weight profile' and this was not so. Breaches of the Code were ruled. This aspect of the ruling applied to all three cases. In Case AUTH/2538/10/12 the claims about Seroquel and weight in the presentations at issue had been ruled not to be in breach of the undertaking given in the 2010 cases cited by AstraZeneca as they were not closely similar. The Panel also noted AstraZeneca's statement in relation to the present case, Case AUTH/2572/1/13, that the reasons for the alleged breach of Clause 7.2 were unclear.

AstraZeneca had requested the opportunity of further response if the Panel disagreed with AstraZeneca's arguments. The Panel noted that there was no mechanism under the Constitution and Procedure in this regard.

The case preparation manager, having considered AstraZeneca's position very carefully, had determined that the case should be referred to the Panel. This was in accordance with the Constitution and Procedure. The Panel noted that as the papers had been provided to the Panel, the case preparation manager was satisfied that the requirements of Paragraph 5.2 of the Constitution and Procedure had been met: namely the present case was not covered by any of the previous cases, ie Case AUTH/2538/10/12 which concerned the five presentations and an alleged breach of undertaking or Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10 which concerned a Seroquel journal advertisement. The complainant had made it clear that his/her present complaint was not about an alleged breach of undertaking. The Panel noted that its sole function under the Constitution and Procedure was to determine whether there had been a breach of the Code based on the materials provided by the complainant and the respondent. It could not revisit earlier decisions made by the case preparation manager.

The Panel did not accept the company's assertion that the subject of the complaint was a statement made by AstraZeneca in its response to Case AUTH/2538/10/12 and therefore outside the scope of the Code. The complaint now to be considered was about AstraZeneca's statements in relation to weight and Seroquel in the five presentations and whether these were a balanced and fair reflection of the evidence available at the time.

The Panel noted that the complainant had not highlighted specific slides. In Case AUTH/2538/10/12 eight slides in the presentations at issue which contained claims about Seroquel and weight had been identified by the Panel in relation to the alleged breach of undertaking. It was the Authority's responsibility to ensure compliance with undertakings. The Panel noted that the circumstances of the present case, Case AUTH/2572/1/13, were different. The Panel noted that the complainant made a general allegation but had not submitted any detailed reasons. Blog postings about Seroquel and AstraZeneca provided by the complainant largely concerned commentary on internal company documents disclosed during US litigation. The complainant did not explain how or which part of these supported the allegation. Some of the postings identified material which contained statements about weight and the company's commercial strategy in this regard. One posting (Driving the brand) noted that the July 2004 'official labelling' for Seroquel on weight gain, discussed clinical trials which demonstrated a statistically significantly greater incidence of weight gain for Seroquel (23%) compared to placebo (6%). An internal undated company email sent before the US approval of Seroquel stated that the magnitude of weight gain at 52 weeks was about 5kg which was more than the short-term six week gain. Whilst some of the blog postings discussed, *inter alia*, general issues about Seroquel and weight there was no mention of the claims identified in the eight slides considered in Case AUTH/2538/10/12 and nor was there detailed discussion of the clinical data. The complainant had not alleged that the claims were in breach of the Code for the reasons set out in Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10. These being that the presentations stated or implied that Seroquel was the only atypical antipsychotic with a favourable weight profile or that it had a clear advantage in this regard. The Panel noted that, as set out in the introduction to the Constitution and Procedure, a complainant bore the burden of proving their complaint on the balance of probabilities.

The Panel was concerned that AstraZeneca had not responded to the substantive allegation that the presentations were not a fair and balanced reflection of the evidence available at that time. The Panel noted the company's submission that any response in relation to Clause 7.2 would be no more than a reiteration of an argument put forward by the company in 2010 which was unsuccessful resulting in a ruling of a breach of Clause 7.2 (Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10). The Panel noted its general comments above in this regard. In particular, the Panel noted that the statements about Seroquel and weight in the presentations at issue did not state or imply that Seroquel was the only atypical antipsychotic with a favourable weight profile and were thus different to the material previously considered.

The Panel noted that it was not for the Panel to infer detailed reasons to support the allegation on behalf of the complainant. It was for the complainant to establish his case on the balance of probabilities. The Panel considered that the very general nature of the complaint was such that for the reasons set out above the complainant had not discharged his burden of proof and the Panel on this narrow ground ruled no breach of Clause 7.2 of the Code. This ruling was appealed by the complainant.

During its consideration of this case, the Panel noted that effective self-regulation depended, *inter alia*, on the provision of a complete response to a complaint. The Panel was, therefore, concerned that AstraZeneca had failed to provide a substantive response to the complaint. The Panel, however, noted the exceptional background and circumstances to the present complaint and decided, on balance, that whilst it remained concerned about AstraZeneca's conduct, it would not formally report AstraZeneca to the Code of Practice Appeal Board under Paragraph 8 of the Constitution and Procedure for it to consider whether further sanctions were appropriate.

APPEAL FROM THE COMPLAINANT

The complainant provided a report written by a retired US psychiatrist (noted above as the author of the blog articles), which he stated formed the basis of his appeal.

The retired psychiatrist noted his blog postings were in a series called 'Selling Seroquel'. The complaint involved five presentation slide sets from AstraZeneca that were annual business reviews for 1999, 2001, 2002, 2004 and 2006 and had to do with specific slides that mentioned weight gain. The blog, was written as the retired psychiatrist began to look at the devious ways the pharmaceutical industry sold its wares, but he did not think it was the one that mattered for the complaint, that was a series that came called 'Seroquel'. The retired psychiatrist provided links to nine blog articles on Seroquel.

The retired psychiatrist provided links to four more articles on Seroquel and stated that these articles were his review of the studies submitted to the FDA for approval. The retired psychiatrist submitted these articles specifically related to the complaint – adverse effects and weight gain:

The retired psychiatrist noted from the Panel ruling that it appeared that the Panel wanted the complainant to specifically address these slides and relate the evidence to them. The problem was that by the time these slides came around, the story was already in its middle chapters. AstraZeneca knew it had a weight gain problem back in 1997. In the blog article titled 'Seroquel IX: weighty matters ...' the retired psychiatrist stated that he/she had listed some of the many references to weight gain in the FDA analysis for approval.

The retired psychiatrist alleged that the medical person in charge of Seroquel at AstraZeneca had skillfully danced around the weight gain in the published reports and in the FDA submission:

In **Trial 0006**:

'Treatment with ICI 204,636 was associated with clinically significant weight gain (an increase of 7% or more from baseline weight) in 25% of patients compared with 4% of placebo-treated patients. Average weights at endpoint represented a change from baseline of +5.5kg for ICI 204,636-treated patients and +0.5kg for patients in the placebo group... Patients treated with ICI 204,636 gained, on average, 3.1kg, and 24% had clinically significant increases in body weight of 7% or more. **However, weight gain is not uncommon in schizophrenic patients treated with antipsychotic agents and has been reported in as many as one-third of patients treated with clozapine.'**

In **Trial 0008**:

'Treatment with quetiapine was associated with clinically significant weight gain (an increase of >7% from baseline weight) in 25% of the patients in the high-dose group compared with 16% in the low-dose group and 5% in the placebo group... Patients treated with quetiapine had a mean weight gain of 2kg, compared with 0.1kg for patients in the placebo group; **however, weight gain did not necessitate withdrawal of treatment for any patient and may or may not have been clinically important during the 6-week period. Often weight gain in patients treated for acute psychosis seems more a function of a return to pre-exacerbation status and other aspects of well-being associated with improvement in psychosis rather than of treatment.'**

In **Trial 0013**:

'Mean increases in weight with quetiapine, from low to high dose, were +0.9, +2.9, +2.0, +2.6, and +2.3kg, respectively, and were greater than those seen with haloperidol (+0.3kg) or placebo (-0.8kg). Increases from baseline of 7% or greater were considered clinically significant and were seen in greater proportions of quetiapine-treated patients: from low to high dose in 11%, 17%, 10%, 16%, and 13% versus 4% with haloperidol and 6% with placebo. Changes did not necessitate treatment withdrawal or appear dose-related on the basis of descriptive statistics... Although quetiapine was associated with a greater mean weight gain compared with haloperidol and placebo, no patients were withdrawn as a result. When reported as an adverse event, weight gain appeared to be related to dose, but no clear dose-response relationship was evident relative to clinically significant weight gain. Generally mean increases were greater at day 42 for patients who completed the trial (1.5-4.5kg) than for patients who withdrew. **In any case, weight gain over a 6-week period may or may not be clinically significant given that it may be a function of well-being resulting from improvement in psychosis.'**

And in the **Trial 0015** Report they sent the F.D.A.:

'There also appeared to be a dose-related increase in the proportion of patients with clinically significant weight gain among Seroquel groups. **Clinically significant weight gain, which was associated with Seroquel treatment, is often seen during treatment with antipsychotic agents.'**

The retired psychiatrist stated that the AstraZeneca medical employee's boss had, in fact, complemented her on her skill in 'smoke and mirrors' in an internal memorandum dated February 1997.

The retired psychiatrist submitted that the AstraZeneca medical employee's boss had referred to Study 15, a disaster that showed Seroquel's inferiority to Haldol and his/her words about weight gain. But the most telling document was an email dated August 1997 where he/she reflected on the weight gain story after being told that AstraZeneca was going to go with 'weight neutral':

'I couldn't attend the Serebral meeting yesterday and haven't been able to catch up with anyone who had in order to hear what the discussion was opposite weight gain (I suspect no one had read the documents) but I did have a chance to look over [named individual] document and have a couple of comments/thoughts. Perhaps we can chat afterwards?

The purpose of this analysis is 2-fold:

1) Is there a competitive advantage for Seroquel, re-weight gain which we can articulate in posters/talks/vis aids? We know we have weight gain but is it limited to the short-term treatment and flattens out over time? Clozapine continues to accumulate.
2) If not #1, then what do we tell the doctors when they ask about long term weight gain?

I recognize that there are a number of interactions/ confounds in the analyses [named individual] did, but despite this I was really struck by how consistent the data was. Across pools (all trials, 15 alone, all trials – 15), across parameters/measures (mean change from baseline, %change from baseline, proportion which clinically significant weight gain), and across cohorts *various durations of treatment) the results seem to be consistent and show:

Weight gain in more rapid initially

While weight gain slows over the longer term (I only considered to 52 week) there still is weight gain. It doesn't stop…the slope just appears to change.

The magnitude of weight gain at 52 weeks (regardless of pool or cohort) is about 5kg which is more than the short-term 6 week weight gain.

The proportion of patients with clinically significant weight gain at 52 weeks (regardless of pool or cohort) is about 45% and this is more than the % at 6 weeks.

This was quite surprising to me (not the weight gain but the consistency).

Therefore I'm not sure there is yet any type of competitive opportunity no matter how weak. Quantitative comparisons between compounds (clozapine, olanzapine) not from the same trials are seriously flawed. (Not that I would be giving up on an abstract but it requires more though before making a decision that this something we bally-hoo!) I have yet to recheck out the weight gain over time in the haloperidol group in 15 but comparisons here would be pretty shady!

The other issue of what we tell the sales force is more problematic because of the confounds. I feel the urge to delve more deeply into this but I realize resources are constrained, there are substantial limitations to the database and I'm not sure that the answers will be much different.

Thoughts are:

It appears on the scatterplot with slope marked that patients with lower body weights had a greater weight gain. (Note that [another named pharmaceutical company] has made this type of an argument stating that patients starting treatment at less than ideal body weight for frame size [they collect height information which we didn't] gained more weight. We can't draw these conclusions so convincingly.) Could the effect of sex be related to baseline weights of men and women?

If I recall from CTRs, our women are generally heavier.

Could the interaction with age be confounded by sex or even baseline weight?

We know that weight gain is dose related. Does the fact that during the first 6 weeks of treatment in many trials many patients were on low doses and when they got into OLE they may have shifted the dose upward (OLE was flexibly dosed) and therefore delayed the appearance of weight gain appearing as an effect of time on drug? Would analysis of Study 14, the only trial with flexibly dosed acute treatment which offered long term OLE be of help here?

The effect of trial isn't surprising. Is it worth repooling like with like?

For example, perhaps looking just at Studies 12, 13 and 14 which are 6 week acute studies which offered OLE or adding Studies 6 and 8 as well since the populations were similar (Studies 5, 4, 15, 48 and the clin pharm studies with OLE could be argued as having different populations).

I have to keep asking myself, are we going to go through the motions, using precious resources and not really come up with anything more solid for the sales reps?

Comments? Thoughts? Should we get together to chat?

Thanks'

The retired psychiatrist submitted that AstraZeneca certainly knew about the weight gain problems in

1997. Yet AstraZeneca persisted in the equivocation about weight gain. The most telling of the slides referenced by the Panel was the one from 1999 which was essentially a lie. By then AstraZeneca had plenty of information to know it was untrue – for example Study 15 which directly contradicted the zero weight gain implied by this slide.

The retired psychiatrist provided a link to a subdirectory of emails on psychrights that went back and forth about how to hold on to AstraZeneca claims about no or minimal weight gain during the period of the slides in 2001 and 2002 which stated 'weight neutral long term'.

And then in 2000/2001 the retired psychiatrist noted one of his blog articles titled 'Selling Seroquel into the fray'.

The retired psychiatrist submitted that there was a new cloud on the horizon. In 2000, the FDA began to look into the issue of Diabetes in patients on Atypical Antipsychotics and sent them a letter requesting data (an excerpt from AstraZeneca's first response to the FDA was provided).

The retired psychiatrist stated that all of this played into AstraZeneca's long internal discussion about how it could continue to justify the term weight neutral. AstraZeneca played with calling it 'minimal weight gain,' but the retired psychiatrist guessed that didn't sound as good as weight neutral. So this OLE data used for the article was the closest thing AstraZeneca had to a weight neutral data set. The retired psychiatrist stated that he/she had not done justice to all the email traffic as AstraZeneca tried desperately to hang on to weight neutral. AstraZeneca thought it would separate it from Zyprexa, and AstraZeneca was not letting go easily. AstraZeneca had finally ended up putting 'As with other antipsychotics, Seroquel can also be associated with limited weight gain, predominantly during the early weeks of treatment' in its Core Data Sheet, but after the FDA query about Diabetes, AstraZeneca began to discuss removing the word 'limited'.

The retired psychiatrist stated that then somebody at AstraZeneca noticed the obvious – that they had more than just 18 months of data on this group of subjects that had been used for the published paper. The authors had simply cut off the part they didn't like (18 months to four years).

'The mean weight change data beyond 18 months (78 weeks) are, I think, less consistent with a "weight neutrality" story than the data prior to 18 months. I have graphed the data on the attached slide for your review. One note: in the poster and the paper an error was made that is corrected in my graph. In the poster and paper the mean weight gain at 53-78 weeks was given as 1.94kg. From the data tables provided to me it was actually 2.03kg. For the following interval (79-104 weeks) the change was 1.94kg. So I think someone simply and inadvertently misaligned one interval as they transcribed the data. This is only potentially significant in that, with such a misalignment, the next mean weight change that would have been encountered was 3.89kg. It is the data from 3.89kg and subsequent which were omitted from the poster and paper.
The ultimate impact on the reprint carrier is that, in the absence of a valid reason for excluding the data beyond 18 months, I can't endorse the reprint/carrier for promotional use as they may not represent a fair and balanced disclosure of the data available to us. This is, I think, compounded by the failure of the paper (and therefore the reprint carrier) to present the incidence of "weight gain" as an adverse event (4.9%) relative to the incidence of "weight loss" as an adverse event (1.9%). These data also suggest to me that the concept of "weight neutrality" are not supported by these data.

I will be interested in your thoughts as well.'

The retired psychiatrist stated that the reprints didn't make it into circulation after all. While AstraZeneca had discussed removing 'limited', it didn't actually change it for several years. And though the inquiry about Diabetes obviously scared it, AstraZeneca continued to 'defend against potential FDA label threats: QTc, Diabetes' with the same energy that it fought accepting 'weight gain'.

The retired psychiatrist stated that so AstraZeneca, again, knew during the period of the slides in 2001, 2002, and 2004 that its claim of 'weight neutral' or 'favorable weight long-term' were bogus. The only truthful and state of its contemporary knowledge slides in this set were in 2006 where it stated 'less weight gain than olanzapine'.

COMMENTS FROM ASTRAZENECA

AstraZeneca noted that the appeal related to certain weight-related claims made in five presentations stored in the archived materials for investors on AstraZeneca's website; they were archived to comply with AstraZeneca's disclosure policy at the time. The presentations were between 7 and 14 years old and prepared solely for the international investor community and were non-promotional in intent. As the presentations were not in active circulation there were no consequences for health professionals, patients or other companies, and no possibility of influencing prescribing habits. In addition, to reflect the Appeal Board's observations and concerns expressed in Case AUTH/2538/10/12, AstraZeneca had removed the presentations from its website and had added appropriate disclaimers to the media archive content to reflect their historical nature.

AstraZeneca submitted that the complainant was an aggrieved ex-employee; this was one of a series of complaints he had brought before the PMCPA in order to harass AstraZeneca and discredit the company's reputation. More specifically, this complaint directly followed the complainant's 2012 complaint concerning Seroquel weight-related claims in the presentations (ie the same presentations that were the subject of the appeal), and his 2010 complaint concerning weight-related claims expressed in a different forum. It was important, therefore, to briefly summarise the history of this matter.

Case AUTH/2297/1/10

AstraZeneca submitted that the complainant originally complained to the PMCPA in 2010 on weight-related claims. In Case AUTH/2297/1/10 the complainant drew attention to a BBC Radio 4 programme in which he stated that, as a former medical adviser for Seroquel, he was pressurised to approve promotional claims for the medicine which stated that weight gain was not a problem. In addition, he referenced a journal advertisement which stated a weight-related claim for Seroquel. AstraZeneca was ruled in breach of Clauses 7 and 9.1 of the Code; AstraZeneca gave an undertaking to the PMCPA that it would not make the same or similar claims in the future. In an appeal raised by the complainant, the Appeal Board ruled that there had been no breach of Clause 2 of the Code.

Case AUTH/2538/10/12

The complainant complained again in 2012 about weight-related Seroquel claims, this time in the presentations. The complainant referred to Case AUTH/2297/1/10, and alleged in his submission that the presentations made 'false claims', attaching links to the presentations. Despite the statement alleging 'false claims', the Panel treated the matter purely as a breach of undertaking case. The Panel did not ask AstraZeneca to address Clause 7, nor did it request the complainant to contextualise or further clarify his comment (which was surprising considering the lack of any detail supplied by the complainant). Clearly, therefore, the PMCPA did not consider that the content of the presentations warranted an assessment under Clause 7 of the Code.

AstraZeneca noted that the Panel dismissed the complaint in relation to four of the five presentations above, but ruled AstraZeneca in breach of its undertaking in relation to one of the presentations. However, the Panel's ruling was overturned at appeal and as discussed above, the company had taken down the investor relations archive of presentations (including the presentations) from its website and added disclaimers to media archive content.

AstraZeneca noted that the complainant did not appeal the Panel's ruling of no breach in relation to four presentations but did defend the Panel's ruling of a breach in relation to the fifth presentation, again positioning the claims as 'not true'. Instead, the complainant submitted a new complaint about the presentations as explained below.

Case AUTH/2572/1/13

In January 2013, the complainant made his third complaint about AstraZeneca, and referred in his submission to a CBS news article regarding Seroquel; he did not, however, provide any granularity as to the basis and scope of his complaint. Notwithstanding this very unclear position, the Panel merely forwarded the complaint to AstraZeneca asking for a response focused on Clauses 2, 9.1 and 25 of the Code, but notably not Clause 7. It was also of concern that this case was raised in the period between the Panel's initial ruling in Case AUTH/2538/10/12 and the appeal, referencing specific wording within AstraZeneca's response letter of 13 November 2012 (Case AUTH/2538/10/12) as part of the complaint.

AstraZeneca stated that it submitted a comprehensive response which addressed these clauses and raised concerns about the nature and substance of the complaint, and potential implications on process. Consequently, the Panel asked the complainant to provide further detail regarding his allegation. What the complainant provided was, amongst others, a series of links to a personal blog set up by a retired psychiatrist. Subsequently, AstraZeneca was notified that the case preparation manager had made a gross error and had cited the incorrect clauses of the Code to which AstraZeneca should respond, with the case being allowed to proceed as an alleged breach of Clause 7.2 only and AstraZeneca was asked to respond accordingly.

Following review of the complainant's position and AstraZeneca's response, the Panel ruled that AstraZeneca had not breached Clause 7.2 of the Code; the complainant was seeking appealing that ruling.

Detailed response to the complainant's appeal

AstraZeneca submitted that it took its compliance with the Code very seriously. This was why, respectful of the self-regulatory system, AstraZeneca wished to respond to the complainant's appeal.

AstraZeneca recognised that the claims contained in the presentations were specifically different to those ruled in breach in 2010, and respected the fact that this was the position taken by Panel; however, it submitted that Cases AUTH/2297/1/10 and AUTH/2572/1/13 were, in essence (both in meaning and clinically) closely similar, a fact made more relevant by the historical nature of the claims.

AstraZeneca submitted that it would have therefore been disingenuous to have defended the claims in the presentations from 1999 to 2004, on the basis that they were of a historical nature and that, as such, there was no new contemporaneous evidence available to AstraZeneca to build a case other than that already submitted to and considered by the PMCPA in 2010, which resulted in a breach of Clause 7.2 being ruled. AstraZeneca regretted that this position was not clearly enough stated in its response above. The exception was the claim made in the 2006 presentation, where Seroquel was compared with olanzapine, which AstraZeneca did defend and which the complainant stated in his appeal was supported by the data available.

However, and with this in mind, AstraZeneca queried whether, given the procedural concerns raised above Case AUTH/2572/1/13 should have been progressed in the first place.

As explained above, it was AstraZeneca's perception that the complainant had brought this complaint because he had not properly and coherently constructed his case for Case AUTH/2538/10/12. Quite simply, the complainant (with the PMCPA's assistance) should have raised a potential breach of Clause 7.2 of the Code within that case. The PMCPA

certainly had an opportunity to do this, particularly given the complainant's allegation of 'false claims'. In addition, the complainant did not appeal the Panel's findings of no breach in Case AUTH/2538/10/12, despite raising this complaint in the period between the Panel's original ruling and AstraZeneca's appeal. AstraZeneca submitted that allowing the complainant, an aggrieved ex-employee, to use this channel to air his grievances seemed to be a manipulation of the PMCPA's complaint procedure, and amounted to an abuse of process. This was explained further below.

In AstraZeneca's view, this matter had already been adjudicated under the Code, in that the current complaint clearly concerned a matter 'closely similar' to one which had been the subject of previous adjudications by the Panel and the Appeal Board. AstraZeneca acknowledged that in some circumstances a complaint might be allowed to proceed even though it concerned a matter closely similar to one which had been previously adjudicated. However, AstraZeneca understood that this discretionary power should be very narrowly construed and, in its view, this complaint should not have been allowed to proceed under Paragraph 5.2 of the Constitution and Procedure which stated:

'If the complaint concerns a **matter closely similar** to one which has been **the subject of a previous adjudication**, it may be allowed to proceed at the discretion of the Director **if new evidence is adduced by the complainant or if the passage of time or a change in circumstances raises doubts as to whether the same decision would be made** in respect of the current complaint. The Director should normally allow a complaint to proceed if it covers matters similar to those in a decision of the Panel where no breach of the Code was ruled and **which was not the subject of appeal** to the Appeal Board.' (Emphasis added)

AstraZeneca submitted that the present complaint concerned a matter that was 'closely similar' to Cases AUTH/2297/1/10 and AUTH/2538/10/12 and that the matter did not fall within the limited circumstances where the PMCPA had discretion to rule on a matter already adjudicated.

AstraZeneca submitted that in the present complaint, the complainant had not submitted any evidence which was new in that it raised any new issues, or which had come into existence after the adjudication of Case AUTH/2297/1/10 and AUTH/2538/10/12. The complainant's clarified submission included links to the retired psychiatrist's personal blog. His appeal submission included additional links to this blog, and a narrative from the retired psychiatrist citing two emails (which were over 20 years old) obtained in relation to the Seroquel litigation in the US. All of these references were therefore easily available to the complainant when he made his two previous complaints.

AstraZeneca submitted that there was no substantive issue beyond Case AUTH/2297/1/10 and AUTH/2538/10/12 for the Panel and the Appeal Board to adjudicate. As discussed above, a closely similar claim to those in the presentations was previously ruled in breach of Clause 7.2 in Case AUTH/2297/1/10. AstraZeneca submitted that due to the historical nature of these claims, and the fact that they had not been used since 2008, that there was little doubt as to whether the same decision would be made again. Moreover, the discretion available to the PMCPA to adjudicate on complaints closely similar to those previously adjudicated must be narrowly construed. The intention behind the flexibility was clear. Firstly, it was to allow complaints by individuals or companies who had not had the opportunity to appeal the previous ruling. This was clear from commentary in Case AUTH/1233/9/01 which stated that:

'[...] the Constitution and Procedure rather assumed that the party making a complaint about a matter closely similar to a previous complaint would be different to the original complainant.'

Secondly, AstraZeneca submitted that the Panel reserved this flexibility to adjudicate on live issues which had potential consequences for health professionals and patients.

AstraZeneca submitted that in this case, neither of those considerations applied. The complainant could have appealed the Panel's ruling regarding the presentations in Case AUTH/2538/10/12. Further, the presentations were old documents which had been removed from the AstraZeneca website and even before that happened they were extremely difficult to access. The presentations had not been tagged and so very difficult to find on the internet without prior specific knowledge of their content; they had been held in a website archive and had been difficult to find within the website (a minimum of four clicks was needed to get to the content from the website homepage). The issues in front of the Appeal Board were therefore not relevant to today's clinical practice. This was why it was not appropriate for the PMCPA to use its discretion to allow this case to proceed.

AstraZeneca submitted that it seemed that the presentations were only of interest to an aggrieved complainant who had a particular agenda and who knew what he was looking for. The PMCPA should not facilitate this type of complaint by overly accommodating such individuals.

AstraZeneca submitted that whilst not a court of law, the PMCPA was a quasi judicial body entrusted with ensuring fairness and that the general principles of justice were followed so that a company did not have to defend the same subject matter, on the same grounds, brought by the same party, indeterminately (ie the principle of 'a matter already judged'). Any obligation to re-examine a case must clearly be an exception to the principle of legal certainty and so must be interpreted narrowly.

Further, AstraZeneca noted that the Panel re-defined the whole scope of this complaint after AstraZeneca had already submitted a comprehensive response; this was wholly without process and prejudicial to AstraZeneca's ability to appropriately defend itself against historical allegations brought about by an aggrieved ex-employee.

Conclusion

AstraZeneca submitted that none of the issues now raised by the complainant were new with regard to the weight-related claims for Seroquel. It was wholly unreasonable that AstraZeneca should have to invest considerable time and resource defending claims made in historic, non-promotional presentations, where both the claims in essence and the presentations themselves had already been the subject of a detailed review by the PMCPA, and the Appeal Board, in Case AUTH/2297/1/10 and AUTH/2538/10/12 respectively. In any event, AstraZeneca had removed the presentations from the website after the Appeal Board's ruling in Case AUTH/2538/10/12.

AstraZeneca considered that the PMCPA should exercise caution to avoid providing a platform for resentful ex-employees with questionable motives to continue harassing their former employers. Whilst AstraZeneca recognised the importance of employees being able to raise issues and concerns with the PMCPA, but submitted that the Authority was allowing such repeated and unstructured complaints to progress which encouraged the attitude that these types of complaints were acceptable.

AstraZeneca submitted that the complainant would persevere with this form of harassment of AstraZeneca until the PMCPA assisted it in putting a stop to it. The present complaint was an improper manipulation of the complaint procedure by an aggrieved ex-employee.

FINAL COMMENTS FROM THE COMPLAINANT

The complainant was disappointed that AstraZeneca had made a personal attack on him and his motives for bringing this case.

The complainant asked the Appeal Board to focus on the retired psychiatrist's dissection of the claims made in the slides in question.

APPEAL BOARD RULING

The Appeal Board noted that in a previous case (Case AUTH/2538/10/12) the complainant had unsuccessfully alleged that the five presentations at issue, dated 1999, 2001, 2002, 2004 and 2006 respectively, were in breach of the undertaking given in Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10. (These cases concerned a Seroquel journal advertisement published in April 2004 which included an implied claim of no weight gain; breaches of Clauses 7.2, 7.4 and 7.9 were ruled).

The Appeal Board noted that alleged breaches of undertaking were taken up with the Director nominally acting as the complainant as the PMCPA was responsible for ensuring compliance with undertakings. The current case (Case AUTH/2572/1/13), however, was different as it concerned an alleged breach of Clause 7.2 in which the Panel made its rulings based on the parties' submissions. The burden was on the complainant to show, on the balance of probabilities, that a breach of the Code had occurred. Neither the Panel nor the Appeal Board were investigative bodies. In that regard the Appeal Board was concerned that the complainant had not clearly identified the claims at issue and, in relation to each, set out a concise explanation and discussion of the data to support his allegation.

The Appeal Board was concerned that the nature of the material before it was such that it was not always clear how/whether the material supported the complainant's allegation. Extracts from emails and excerpts from published papers were provided. The context of such material was unclear. The Appeal Board had to decide how much weight to attach to this evidence bearing in mind the above.

The Appeal Board noted that the Seroquel summary of product characteristics (SPC) dated 19 April 1999 stated in Section 4.8 Undesirable Effects, that 'As with other antipsychotics, Seroquel may also be associated with limited weight gain, predominantly during the early weeks of treatment.' A closely similar statement was included in the August 2002 SPC. By November 2006 'limited' had been removed and the statement now read 'As with other antipsychotics, Seroquel may be associated with weight gain, predominantly in the early weeks of treatment.'

The Appeal Board noted that the claims about weight in the presentations at issue were as follows: 'Seroquel - minimal weight gain' (1999); 'weight neutral in the long term' (2001); 'Weight-neutral long-term' and 'weight-neutral in the long term' (2002); 'Favourable weight profile long-term'(2004); 'Less weight gain than with olanzapine' (2006). The Appeal Board noted that the complainant considered that the latter comparative claim was truthful.

The Appeal Board considered that there was insufficient evidence provided by the complainant to show that the presentations, when written, did not provide a fair and balanced reflection of the evidence available at the time regarding weight gain with Seroquel. The Appeal Board considered that the complainant had not discharged his burden of proof and it upheld the Panel's ruling of no breach of Clause 7.2. The appeal was unsuccessful.

Complaint received **15 January 2013**

Case completed **26 June 2013**

EX-EMPLOYEE v GEDEON RICHTER

Sponsorship to attend an international meeting

An ex-employee complained about the sponsorship of UK health professionals to attend the International Federation of Gynaecology and Obstetrics (FIGO) conference in Rome, October 2012.

The complainant stated that Preglem had invited doctors from all over Europe including the UK. The complainant noted that Preglem sponsored a very large number of UK clinicians to go to the FIGO conference and queried how this was certified at this expense.

The detailed response from Gedeon Richter is given below.

The Panel noted that Gedeon Richter had sponsored 33 UK health professionals to attend FIGO in Italy in October 2012.

The Panel examined the information provided by Gedeon Richter UK. The cost per person to include flight, accommodation and dinners on five nights ranged from around £1,866 for a health professional who stayed 6 nights, to around £771 for a health professional staying 2 nights. The hotel cost at £196 per night seemed high, however it noted that the conference was held in Rome. The costs for dinners were, in the main, reasonable. One evening had cost around £63 on average and this was considered to be on the high side bearing in mind the requirements of the Code. On balance, the Panel did not consider that the costs for travel, accommodation and subsistence overall were unacceptable as alleged and no breach of the Code was ruled.

An ex-employee of Preglem UK (a wholly owned subsidiary of Gedeon Richter) complained about the sponsorship of UK health professionals to attend the International Federation of Gynaecology and Obstetrics (FIGO) conference in Rome, 7-12 October 2012.

COMPLAINT

The complainant stated that Preglem had invited doctors from all over Europe including the UK.

The complainant submitted that Preglem sponsored a very large number of UK clinicians to go to the FIGO conference and queried how this was certified at this expense.

When writing to Gideon Richter the Panel asked it to respond in relation to Clause 19.1 of the Code.

RESPONSE

Gedeon Richter (UK) Ltd explained that Preglem SA, based in Geneva, was a wholly owned subsidiary of Gedeon Richter whose headquarters were in Budapest.

The arrangements relating to the invitation and attendance of UK health professionals at the conference were subject to full review and approval by the UK company in line with the requirements of the Code.

Gedeon Richter noted that the complainant described the number of UK clinicians sponsored by the company to attend the conference as 'very large' and implied that the expense associated with such sponsorship was in some way unreasonable.

FIGO was a highly prestigious international meeting which occurred every three years. It was 5 days of lectures and posters and a unique opportunity for those working in obstetrics and gynaecology to network and update themselves with international opinion and clinical research. In 2012 more than 8,000 delegates from around the world attended the meeting in Rome.

In the UK there were 3,672 physicians (consultants and registrars) in the field of obstetrics and gynaecology, according to the Royal College of Obstetricians and Gynaecologists. Of this group the UK company invited 33 consultants/professors to attend FIGO 2012. Some delegates attended for the full 5 days of the meeting and some for less according to available study leave. All travel to the congress was by economy and mostly via budget airlines. Accommodation was arranged in a business style 4 star hotel some 40 minutes from the congress venue. All restaurants selected were in the lower mid-range of those available in Rome and gave reasonable levels of subsistence commensurate with that which the company would have selected in the UK for a congress dinner. The company provided a spreadsheet.

The average cost per UK delegate including accommodation, flight and subsistence was £1,402.05 (range £793.69 to £1,865.59 depending on length of stay). All other incidental costs were settled by the delegates as stated in the invitation letter (copy provided).

Gedeon Richter did not consider that the number of UK delegates invited to attend the meeting nor the costs associated with their attendance were unreasonable or inconsistent with the requirements of the Code.

In conclusion, Gedeon Richter strongly refuted any suggestion that any of the arrangements by the UK company to sponsor UK health professionals to attend the FIGO meeting in Rome in October of 2012 were in any way inconsistent with the requirements of the Code.

PANEL RULING

The Panel noted that Gedeon Richter had sponsored 33 UK health professionals to attend FIGO in Italy in October 2012.

The Panel reviewed relevant requirements of the Code in relation to meetings, hospitality and sponsorship and Gedeon Richter UK's responsibility.

Clause 19.1 stated that 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 costs involved must not exceed that level which the recipients would normally adopt when paying for themselves. The supplementary information to Clause 19.1 made it clear that the provision of hospitality was limited to refreshments/ subsistence, accommodation, genuine registration fees and the payment of reasonable travel costs which a company might provide to sponsor a delegate to attend a meeting. The venue must not be lavish, extravagant or deluxe and companies must not sponsor or organise entertainment such as sporting or leisure events. In determining whether a meeting was acceptable or not consideration needed to be given to the educational programme, overall cost, facilities offered by the venue, nature of the audience, subsistence provided and the like. It should be the programme that attracted delegates and not the associated hospitality or venue. The supplementary information also stated that a useful criterion in determining whether the arrangements for any meeting were acceptable was to apply the question 'would you and your company be willing to have these arrangements generally known?' The impression that was created by the arrangements for any meeting must always be kept in mind.

The Panel examined the information provided by Gedeon Richter UK. The cost per person to include flight, accommodation and dinners on five nights ranged from around £1,866 for a health professional who stayed 6 nights, to around £771 for a health professional staying 2 nights. The hotel cost at £196 per night seemed high, however it noted that the conference was held in Rome.

The costs for dinners were, in the main, reasonable. One evening had cost around £63 on average and this was considered to be on the high side bearing in mind the requirements of Clause 19. On balance, the Panel did not consider that the costs for travel, accommodation and subsistence overall were unacceptable as alleged and no breach of Clause 19.1 was ruled.

Complaint received **25 January 2013**

Case completed **22 April 2013**

CASE AUTH/2574/2/13

PHARMACIST v SANOFI PASTEUR MSD

Promotion of Zostavax

A senior primary care pharmacist, complained about an email from a Sanofi Pasteur MSD representative to a general practice which referred to supplies of Zostavax (varicella-zoster virus (live)). Zostavax was indicated for the prevention of herpes zoster (shingles) and herpes zoster-related post-herpetic neuralgia (PHN).

The email referred to Zostavax, the national programme for immunising certain patients and the opportunity to maximise on profit for the surgery (£26 per dose profit now compared to enhanced payment of around £7 from September). A letter template to invite patients for the shingles vaccine was provided. The email stated that this invitation had been very well received and had allowed surgeries to set up dedicated clinics.

The complainant stated that he/she and his/her colleagues considered that encouraging GPs to prescribe for profit was inappropriate and queried whether such was in breach of the Code with regard to inducement.

The detailed response from Sanofi Pasteur MSD is given below.

The Panel noted that the definition of promotion excluded measures or trade practices relating to prices, margins or discounts which were in regular use by a significant proportion of the pharmaceutical industry on 1 January 1993. Further the supplementary information to the Code Terms of Trade stated that such measures or trade practices were excluded from the provisions of that clause. The terms prices, margins and discounts were primarily financial terms. The Panel noted that other trade practices were subject to the Code and had to comply with it.

The Panel noted that the email in question had been sent by one representative to practice managers. It encouraged practice managers to maximize profit by ordering Zostavax for patients 50-69 and 80 years old ahead of the introduction of the national programme for patients 70 to 79 years of age. The email also referred to the vaccine's protection. The email did not quantify the discount but made it clear that practices would, in effect, earn £26 per dose profit for each patient vaccinated now compared to around £7 from September when the national programme started. Any unused vaccine could be returned at no cost. The email included a template letter for the practice to send to patients and referred to the establishment of vaccine clinics.

Whilst the Panel had some concerns about the email, taking all the circumstances into account and on balance the Panel decided that as the arrangement related to the cost of the vaccine ie financial terms it could take the benefit of the exemption for terms of trade and no breach was ruled.

The Panel was, nonetheless, concerned about the impression given by the letter. It appeared to advocate vaccinating certain groups of patients primarily on the basis of profit to the surgery. The Panel noted the complainant's view that the impression of encouraging GPs to prescribe for profit was inappropriate. The email and template letter had been sent to practice managers without the company's knowledge or approval. The Panel considered that high standards had not been maintained and a breach was ruled. The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such circumstances.

A senior primary care pharmacist, complained about the promotion of Zostavax (varicella-zoster virus (live)) by a representative from Sanofi Pasteur MSD. Zostavax was indicated for the prevention of herpes zoster (shingles) and herpes zoster-related post-herpetic neuralgia (PHN).

COMPLAINT

The complainant referred to an email from a Sanofi Pasteur MSD representative to a general practice which read:

> 'I just wanted to give you an update on Zostavax, any quantity of Zostavax purchased has 100% sale or return on it. 40 doses would get you the maximum discount and current stock has an expiry of 28th Feb 2013. The National programme will start in September 2013 for patients 70-79 years of age. Now is the opportunity to catch your 50-69 and 80 year old's (and those turning 80 before September) to give patients protection and to maximise on profit for the surgery (£26 per dose profit now compared to enhanced payment of around £7 from September). Many of our surgeries are doing this now and have been able to vaccinate 20 patients plus a day and it is proving to be very successful. Please find attached the letter template to get your patients in for the shingles vaccine. This invitation has been very well received which has allowed surgeries to set up dedicated clinics to have patients vaccinated.'

The complainant stated that he/she and his/her colleagues considered that encouraging GPs to prescribe for profit was inappropriate and queried whether such was in breach of the Code with regard to inducement.

When writing to Sanofi Pasteur MSD the Authority asked it to consider the requirements of Clauses 2, 9.1 and 18.1 of the Code.

RESPONSE

Sanofi Pasteur MSD stated that it was committed to maintaining high standards in promoting its vaccines and always strove to comply with the Code. The company was thus very concerned about the complainant's allegations and had endeavoured to investigate the matter thoroughly.

In summary, Sanofi Pasteur MSD considered that the UK Human Medicines Regulations 2012 and Clause 1.2 (and accordingly the supplementary information for Clause 18.1) permitted trade practices relating to discounts. Accordingly, the company's discount arrangement was consistent with relevant UK regulations, did not constitute an inducement to prescribe and was not in breach of Clause 18.1.

Sanofi Pasteur MSD submitted that it had processes and policies in place with regard to the use of emails and promotional materials in order to maintain high standards in the promotion of its vaccines, consistent with the underlying principles set out in Clause 9.1. The representative's conduct was an isolated act. The company took this matter very seriously and upon learning of the complaint, immediately reminded employees of its established processes and policies.

As the email had not prejudiced patient safety or public health, nor served as an inappropriate inducement to prescribe as set out in the supplementary information for Clause 2, the activities or materials associated with the promotion of Zostavax could not be properly considered as falling within the scope of a censured act contemplated by Clause 2.

With regard to Clause 18.1, Sanofi Pasteur MSD noted that the provision of discounts was allowed under the Code. The Human Medicines Regulations 2012, Regulation 300(6) and specifically Clause 1.2 of the Code allowed promotional activity in relation to 'trade practices relating to prices, margins or discounts which were in existence on 1st January 1993'. These were primarily financial terms and normally covered cash discounts or equivalent business discount schemes on purchases of medicines, including volume discounts provided they were clearly identifiable and invoiced.

Past cases had consistently confirmed this position, specifically in relation to volume based discounts:

- Case AUTH/2371/11/10 - the Panel considered that discussions on discounts could be made together with promotion of medicines.

- Case AUTH/2230/5/09 - the Panel ruled that a complainant had the burden of proving their complaint on the balance of probabilities. Although it noted the serious allegation, the Panel did not consider that the complainant had provided evidence to show that, on the balance of probabilities, the representative had offered discounts during the course of promotion such that the arrangements amounted to an inducement to prescribe the company's products. The Panel thus ruled no breach of the Code.

- Case AUTH/2272/10/09 - the Appeal Board considered that discount schemes would result in more prescriptions of a company's product and clarified that the schemes were not necessarily unacceptable as long as the arrangements complied with the Code. In that case, a primary care organisation would potentially qualify for a larger rebate if its prescribers increased the number of packs of the company's products they prescribed.

Therefore, Sanofi Pasteur MSD believed that its volume-based discount structure was permissible under the Code and the UK Human Medicines Regulations. Such discount structures were, and had been for many years (and certainly before 1993), a standard trade practice and were used widely in the vaccine industry. Sanofi Pasteur MSD provided examples of discount schemes offered by other vaccine manufacturers taken from publicly available sources and submitted that the NHS understood discounts to be part of normal trade practices.

Vaccines such as Zostavax, which were not part of a national vaccination programme, could be purchased and, in certain circumstances dispensed by GP practices. After these GP practices had purchased the vaccine, almost always at a volume based discount, the surgery would seek reimbursement for the list or NHS price of the medicine, as laid out in 'GMS statement of financial entitlements'.

However, the NHS reserved the right to impose a clawback (refund) of some of these discounts from the GP practice and had established a clawback rate of £11.18 per dose for Zostavax. The existence of this clawback demonstrated that the NHS expressly recognised that discounting was expected when surgeries bought Zostavax. Indeed, the receipt of a discount would be necessary if a GP practice was to be able to offer this vaccination service to patients as they would have to acquire the vaccine at £88.78 (list price £99.96) to just break even. There would of course be additional costs to the practice incurred in prescribing and then administering the vaccine (usually at a separate clinic run by the practice nurse) so the additional discount would justifiably reflect the cost associated with providing the service.

The email must, therefore, be considered in this context. It was sent to practice managers whose role involved the financial management of the practice which might include the purchase of medicines for personal administration. As the email was commercial in nature and did not refer to the clinical benefits of Zostavax, it would only be relevant to individuals who had a commercial role and were empowered to make purchasing decisions that were financially viable. Such individuals would naturally be interested in receiving information about discounts available from vaccine manufacturers.

In view of the above, Sanofi Pasteur MSD considered that the discount offered by the representative was an acceptable trade practice as contemplated by the Code and was not an inducement to prescribe. The company thus denied a breach of Clause 18.1.

With regard to Clause 9.1, Sanofi Pasteur MSD submitted that it had provided comprehensive training for its staff with regard to adherence to the Code and had strict policies in place in relation to the approval of promotional materials and the use of emails. Training on the Code was compulsory for all members of staff, with specific training programmes for representatives. Knowledge of field-based staff was assessed via an accreditation process on completion of the training. The representative who sent the email at issue had fully completed his/her training on the Code and had received updates on the changes to the Code in 2012.

Sanofi Pasteur MSD stated that its policy on communication with customers prohibited employees from using these forms of communication promotionally; any deviation from this policy was considered a serious matter.

Sanofi Pasteur MSD stated that it had determined that the email in question and the letter template were prepared and sent by one representative. The representative had acknowledged in his/her disciplinary meeting that his/her actions violated company policies and procedures and that he/she had acted alone.

Neither the email nor the letter template was reviewed or sanctioned by the company. Indeed, Sanofi Pasteur MSD had not prepared any letter template inviting patients for shingles vaccination. The independent drafting and sending of this email was completely contrary to how the company expected and trained its representatives to act. Company procedures strictly prohibited representatives from preparing their own promotional materials. The company took this deviation very seriously and had carried out the following actions:

- Using key search words and phrases, a search of all emails sent from staff was conducted to confirm whether the email sent to the complainant was an isolated incident. Based on this search and the representative's own admission, Sanofi Pasteur MSD believed that this representative was the only staff member to send such an email communication.

- A communication had been sent to all representatives to re-emphasise company policy on the prohibition of the use of emails for promotional purposes. The company had also taken the opportunity to reconfirm the adequacy of its procedures.

The company considered it unacceptable for any member of staff to deviate from its policies.

Sanofi Pasteur MSD submitted that its established process and policy on promotion of vaccines was consistent with the underlying principles set out in Clause 9.1.

With regard to Clause 2, Sanofi Pasteur MSD submitted that this incident had not prejudiced patient safety and/or public health. The Human Medicines Regulations 2012, Regulation 300(6) and Clause 1.2 of the Code allowed volume based discounts and the offer of a discount that by its terms constituted an acceptable trade practice could not amount to an inducement to prescribe.

Sanofi Pasteur MSD was committed to maintaining high standards in promoting its vaccines and had appropriate policies and procedures in place to help ensure this. Consequently, the company did not consider that its actions had brought discredit upon or reduced confidence in the industry and therefore it denied a breach of Clause 2.

PANEL RULING

The Panel noted that Clause 1.2 excluded from the definition of promotion measures or trade practices relating to prices, margins or discounts which were in regular use by a significant proportion of the pharmaceutical industry on 1 January 1993. Further the supplementary information to Clause 18.1 Terms of Trade stated that such measures or trade practices were excluded from the provisions of that clause. The terms prices, margins and discounts were primarily financial terms. The Panel noted that other trade practices were subject to the Code and had to comply with it.

The Panel noted that trade practices may have evolved since 1 January 1993. Companies should take particular care to ensure that any trade practice which could not take the benefit of the relevant exemption complied with all the requirements of the Code and in particular Clause 18.1 which included a prohibition on inducement to prescribe, supply, administer, recommend, buy or sell any medicine. In this regard the Panel considered that particular care should be taken in relation to such trade practices and general practice where it might be argued that a personal financial benefit might accrue to the partnership contrary to Clause 18.1. Companies would be well-advised to ensure such trade practices offered to general practice met the requirements of the relevant exemption.

Turning to the case at issue the Panel noted that the email in question had been sent by one representative to practice managers. It encouraged practice managers to maximize profit by ordering Zostavax for patients 50-69 and 80 years old ahead of the introduction of the national programme for patients 70 to 79 years of age. The email also referred to the vaccine's protection for patients. The Panel noted that the email did not quantify the discount but made it clear that practices would, in effect, earn £26 per dose profit for each patient vaccinated now compared to around £7 from September when the national programme came into effect. Any unused vaccine could be returned at no cost. The email included a template letter for the practice to send to patients and referred to the establishment of vaccine clinics.

Whilst the Panel had some concerns about the email, taking all the circumstances into account and on balance the Panel decided that as the arrangement related to the cost of the vaccine ie financial terms it could take the benefit of the exemption to Clause 18.1,

Terms of Trade. Thus the Panel ruled no breach of Clause 18.1.

The Panel was nonetheless concerned about the impression given by the letter. It appeared to advocate vaccinating certain groups of patients primarily on the basis of profit to the surgery. The Panel noted the complainant's view that the impression of encouraging GPs to prescribe for profit was inappropriate. The email and template letter had been sent to practice managers without the company's knowledge or approval. The Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled. The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such circumstances.

Complaint received **1 February 2013**

Case completed **26 April 2013**

CASE AUTH/2575/2/13

EX-EMPLOYEE v GEDEON RICHTER

Promotion of Esmya

An ex-employee of Preglem (a wholly owned subsidiary of Gedeon Richter) complained prospectively about the promotion of Esmya (ulipristal acetate) at a meeting to be held in Barcelona, April 2013.

The complainant referred to an invitation to health professionals which was available on a publicly accessible website. The invitation/save the date document referred to Esmya, its generic name, its indication and to Barcelona. The meeting venue was not stated. The complainant alleged that the invitation appeared to promote Barcelona rather than the meeting itself. The registration link and the access code also referred to Barcelona.

The complainant noted that the invitation referred to 'new phase III evaluating the safety and efficacy of ulipristal acetate in the treatment of uterine fibroids'. The complainant submitted that if this was phase III data, then it would amount to promoting off-label as the licence would not be obtained before the meeting. The complainant further noted that the material was approved in January 2013 but there was no medical signatory available then to certify this foreign travel.

The complainant noted that the events company organising the Barcelona meeting had several invitations from Gedeon Richter on the past events section of its website. Some invitations included the name of the medicine and its indication. The complainant alleged that this seemed like a concerted effort to promote a prescription only medicine to the public.

Finally, the complainant noted that Gedeon Richter also held a meeting in Barcelona in March 2012. The invitations were similar to those for the 2013 meeting but were sent before the grant of the licence in February 2012.

The detailed response from Gedeon Richter is given below.

The Panel considered that as the front page of the invitation to the April 2013 meeting featured the Esmya brand imagery, recipients would immediately associate the meeting with the medicine. The invitation stated that the meeting was, *inter alia*, about ulipristal acetate for the treatment of uterine fibroids and referred to 'highly scientific and interactive sessions on new phase III clinical data evaluating the efficacy and safety of ulipristal acetate in the treatment of uterine fibroids'. A footnote stated that Esmya 5mg was indicated for the pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age with a treatment duration limited to 3 months. The Panel considered that although the invitation promoted Esmya it did not do so for an unlicensed indication. The statement about new phase III data only referred to the product's use in the treatment of uterine fibroids and details of the indication were included. The Panel ruled no breach of the Code.

The invitation asked recipients to save the 12, 13 and 14 April. According to the programme the meeting started on Friday, 12 April at 14.15 and finished at 17.30. This was followed by dinner. The agenda for 13 April ran from 09.00-12.00.

The Panel was concerned that the invitation implied that the meeting would finish on 14 April. This was not so. As the meeting referred to on the invitation finished at midday on 13 April, the Panel failed to see why delegates had to keep 14 April free. A symposium for UK delegates was arranged from 14.00-17.00 on 13 April. This was not mentioned on the save the date card. The Panel did not know when the company informed the UK delegates about this additional seminar. The Panel noted Gedeon Richter's submission that it had decided to hold the UK seminar before the save the date card was sent. The Panel thus queried why this was not mentioned on the invitation card.

The Panel noted that 18 of the UK delegates had stayed in Barcelona for the night of 13 April as the finish time of the meeting (17.00) meant that a return flight was either impossible or the timing of such was inconvenient. The Panel noted that the delegates' difficulties in getting back to the UK on the Saturday evening appeared to contradict Gedeon Richter's submission that Barcelona was chosen because of its easy travel links. Dinner was provided for those who stayed in Barcelona on the Saturday night. Some delegates had had three nights' accommodation paid. For a few of the delegates this was so that they could catch early flights out of the UK on 12 April. The Panel did not consider that the content of both meetings justified two or three nights' accommodation.

The Panel noted Gedeon Richter's reasons for choosing Barcelona. Speakers and delegates were mainly from European countries. The Panel accepted that for a European meeting many delegates would have to travel but considered the company should have made better use of the time so that no-one needed to stay for two nights. The Panel was concerned about the arrangements. It queried why the meeting for UK delegates had not started sooner than 2 hours after the end of the morning meeting and when delegates had been informed about this meeting; the afternoon session for UK delegates was referred to in the final

confirmation letter to delegates. The Panel was concerned that the save the date card implied that there would be scientific content on the Sunday.

Overall, the Panel considered the arrangements were unacceptable and a breach was ruled. The Panel ruled a further breach as the invitation to the meeting outside the UK had not been certified as acknowledged by Gedeon Richter.

The Panel noted that the invitation had been available on the events company's website and also Gedeon Richter's submission that it was unlikely that anyone would stumble upon it without being directed by other means. Health professionals would only be directed to the website if they had received a hard copy of the invitation from a representative. The Panel did not consider that in these circumstances the availability of the invitation on an events company's website constituted advertising a prescription only medicine to the public as alleged and no breach was ruled.

The Panel considered that the rulings of breaches above meant that high standards had not been maintained and that the arrangements brought discredit upon and reduced confidence in the pharmaceutical industry. Breaches of the Code were ruled including a breach of Clause 2.

The Panel was concerned that the save the date invitation for a meeting held in Barcelona on 2/3 March 2012 in effect promoted an unlicensed medicine. The invitation, dated December 2011, referred to Esmya by generic name. The preliminary programme which appeared to have been sent with the invitation included the Esmya product logo and presentations 'How is Esmya different'. The agenda included presentations on Esmya and phase III data. The Panel noted that according to its summary of product characteristics (SPC), Esmya was first authorized in February 2012. The Panel considered that both the agenda and the preliminary programme promoted an unlicensed medicine and a breach was ruled. High standards had not been maintained and a breach was ruled.

On balance, the Panel did not consider the circumstances warranted a ruling of a breach of Clause 2 of the Code which was reserved for use as a sign of particular censure.

An ex-employee of Preglem (a wholly owned subsidiary of Gedeon Richter) complained prospectively about the promotion of Esmya (ulipristal acetate) at a meeting to be held in Barcelona, April 2013.

Esmya 5mg was indicated for pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The duration of treatment was limited to 3 months. The summary of product characteristics (SPC) stated that the marketing authorization holder was Gedeon Richter plc Budapest. The Esmya SPC stated that the product was an orally active synthetic selective progesterone receptor modulator (SPRM) and was first licensed in February 2012.

COMPLAINT

The complainant referred to an invitation to health professionals which was available on a publicly accessible website and provided the relevant link. The complainant noted that the invitation/save the date document referred to Esmya, its generic name, its indication and to Barcelona. There was no mention of the venue where the meeting would be held. The complainant alleged that the invitation appeared to promote Barcelona rather than the meeting itself. In that regard the complainant noted that the registration link and the access code also referred to Barcelona.

The complainant noted that the invitation stated that there would be participation on 'new phase III evaluating the safety and efficacy of ulipristal acetate in the treatment of uterine fibroids'. The complainant submitted that if this was phase III data, then it would amount to promoting off-label as the licence would not be obtained before the meeting.

The complainant further noted that the material was approved in January 2013 but there was no medical signatory available then to certify this foreign travel as the medical signatory had left the company in December 2012.

The complainant noted that the events company organising the meeting in Barcelona had several invitations from Gedeon Richter on its website. Some invitations had the name of the medicine and its indication. The complainant referred in this regard to the 'past events' section of the website. The complainant alleged that this seemed like a concerted effort to promote a prescription only medicine to the public.

The complainant further noted that Gedeon Richter also held a meeting in Barcelona in March 2012. The invitations were similar to those for the 2013 meeting but were sent in January before the grant of the licence in February 2012.

When writing to Gedeon Richter, the Authority asked it to consider the requirements of Clauses 2, 3.1, 3.2, 9.1, 14.2, 14.3, 19.1 and 22.1.

RESPONSE

Gedeon Richter explained that the invitation to the meeting in Barcelona April 2013, sent out to certain health professionals requesting that they save the date in advance of the symposium, clearly informed the recipient of the title and therefore the nature of the meeting before informing them of where the meeting was to be held. The font size was no larger than the font size used for the title of the symposium and the colour of the text was not particularly eye-catching.

Gedeon Richter submitted that it was reasonable to inform clinicians that the meeting would be held overseas as this would provide some idea as to the logistics and domestic impact in terms of absence from home that attendance would be likely to have. It was an international meeting with attendees from many European countries. UK attendees were likely to be a significant minority and so it was reasonable

for them to travel overseas to attend this sort of a meeting.

Given the above, Gedeon Richter refuted the allegation that it had promoted the venue rather than the meeting itself and it thus denied a breach of Clause 19.1.

Gedeon Richter noted that the supplementary information to Clause 3 that 'The legitimate exchange of medical and scientific information during the development of a medicine is not prohibited provided that any such information or activity does not constitute promotion which is prohibited under this or any other clause'. The Barcelona meeting was to act as a forum to allow interested clinicians to discuss SPRMs, of which ulipristal acetate was one, in the overall treatment of uterine fibroids. As the PEARL III study would have completed by the time the meeting was held, it seemed appropriate to include this data in the discussion; this was the 'new phase III clinical data' mentioned in the invitation. Given the position of this information and its relative lack of prominence in the invitation (it only featured mid-way down the invitation, was in black text whereas the programme title was in an eye-catching blue text, and was of a smaller font than the other elements of the invitation) this was clearly not the main focus of the event.

Gedeon Richter further noted that it would be reasonable to expect that the invited clinicians would understand that phase III data by definition represented data that was outside the current licensed indication which was clearly stated in the prescribing information on the back of the invitation. In order to add yet more clarity as to the precise licence of Esmya an asterisk to the title of the symposium drew the reader's attention to the text at the bottom of the page where the therapeutic indication was stated in full. These elements should help to make it clear to clinicians that this was interesting and relevant scientific information but as it was outside the licensed indication, Gedeon Richter did not recommend its use in this manner.

Gedeon Richter considered that the meeting was an opportunity to discuss SPRMs and for interested health professionals to discuss the status quo and data that would be available when the meeting was held and it did not consider that this represented a breach of Clause 3.2.

Gedeon Richter stated that due to a change in company personnel, including the departure of the company's only medical signatory when the invitation was in the final stages of development, it was not possible to demonstrate that the invitation had undergone the complete review and approval process. Gedeon Richter was a small organisation and the departure of the medical signatory clearly had a significant impact on its ability to function though it strove to adhere to the relevant codes of practice. The UK operating company consisted of a medical practitioner, a head of marketing, a financial controller, a team assistant and the managing director, so clearly the departure of even one member of the team introduced potential challenges. In order to allow clinicians enough time to arrange either study leave or annual leave to attend the meeting, it was decided to send out the invitation. A previous version of it had been reviewed by the medical final signatory and non-medical final signatory and amendments were proposed and subsequently made in order to make the piece comply with the Code. Additionally the first version of the invitation was reviewed by two separate reviewers, both of whom either were then or were now registered with the PMCPA as non-medical final signatories. While this did not represent a complete defence to the alleged breach of Clause 14.3, Gedeon Richter stressed that all possible steps were taken in order to comply with the Code.

Gedeon Richter noted that the events company had acted on its behalf to passively facilitate the registration of attendees to a meeting. There were no promotional activities carried out by the events company and as there were no Internet search engine optimisation techniques applied to the company's website, it was extraordinarily unlikely that a health professional or member of the public would stumble upon the invitations without being directed there by other means. Health professionals would only be directed to the events company's website by receipt of a hard copy of the invitation from a Gedeon Richter representative. Further, Gedeon Richter did not consider that the invitation promoted Esmya. While it was mentioned in the invitation as being a treatment for uterine fibroids, there were no specific promotional claims made or elements of the therapeutic indication mentioned. Mention of a medicine and the disease area in which it could be used should not constitute promotion *per se*. Gedeon Richter stated that the complainant was naturally able to access the events management agency website to highlight the presence of the invitation as he/she had prior knowledge of the website that a member of the public simply would not have.

Given the entirely passive nature of the presence of the invitations on the website, the lack of any promotional activity by the events company and the fact that Gedeon Richter did not consider that the mention of ulipristal acetate in the domain of uterine fibroids constituted promotion, the company denied the alleged breach of Clause 22.1.

With regard to the meeting held in Barcelona in 2012, Gedeon Richter reiterated the supplementary information to Clause 3 with regard to the legitimate exchange of medical and scientific information during the development of a medicine.

The March 2012 symposium in Barcelona was planned as an overview of the management of SPRMs and an opportunity to review the profile of ulipristal acetate which was then in the final stages of regulatory approval. The 'Save the date' card mentioned ulipristal acetate but this was in the context of the management of the disease with SPRMs. The preliminary agenda included in the invitation mentioned ulipristal acetate (Esmya) in only 4 of the 10 meeting sessions and the total time dedicated to ulipristal acetate was no more than 50%. The marketing authorization for ulipristal

acetate was granted by the European Medicines Agency (EMA) after the 'Save the date' card and invitation had been sent but before the meeting took place.

Given that Gedeon Richter did not consider that the 'Save the date' card and the meeting invitation were promotional, it denied a breach of Clause 3.1.

Despite the formal lack of medical final certification of the invitation to the symposium to be held in Barcelona in April 2013, Gedeon Richter considered that the steps that were taken to ensure that the invitation complied with the Code demonstrated that it had not failed to maintain high standards.

The company also absolutely refuted the allegation that it had breached Clause 2 as it did not consider, particularly given the nature and origin of the complaint, that it had brought discredit upon, or reduced confidence in, the pharmaceutical industry.

In response to a request for further information, Gedeon Richter submitted that the meeting invitations were offered to consultant gynaecologists interested in the treatment of uterine fibroids as it was considered that they would get the greatest benefit from participating in a scientific meeting with speakers who were considered to be thought leaders in this field. There were no requirements set out to determine eligibility to receive an invitation to attend the meeting and registration was on a 'first come, first served' basis. The invitations were distributed through the field-based team of key account managers either as a hard copy or by email. A similar system was in pace for the 2012 meeting; the target audience was the same group of health professionals and registration was again operated on a 'first come, first served' basis.

Gedeon Richter provided the agendas for the 2012 and the 2013 meetings. The company submitted that there had been few recent developments in the treatment of uterine fibroids so these international scientific symposia were developed to support ongoing scientific discussions and education in this field. They gave interested gynaecologists an opportunity to hear international thought leaders speak about the most up-to-date information on the disease and its treatment. As the vast majority of speakers for both the 2012 and 2013 meetings were not from the UK (as was evident from the agendas for both meetings) it was considered that it would be reasonable to invite UK health professionals to attend the meeting and to facilitate their travel.

Barcelona was chosen as the venue for the two meetings as it had easy travel links to the rest of Europe and a number of venues that could accommodate meetings such as those at issue. The number of UK attendees (53 out of 295 in 2012 and 40 out of 378 in 2013 (attendance figures by country were also provided)) also represented a significant minority so based on this it was considered reasonable to invite UK health professionals to the meeting. While uterine fibroids was an area of unmet clinical need in the UK and the rest of the world, the relative lack of therapies meant that the topic was often under-represented at gynaecology conferences. By bringing together the thought leaders in this branch of gynaecology the 2012 and 2013 meetings offered an opportunity for gynaecologists to expand their knowledge and understanding of the treatment of uterine fibroids. Given that these meetings allowed gynaecologists to gain education in this area it was considered appropriate to invite UK health professionals and indeed, some of those who had attended the 2012 meeting expressed an early interest in attending the 2013 meeting as they considered that it was a valuable learning resource.

In response to a second request for further information Gedeon Richter submitted that following discussion between clinicians and the key account managers about what information the clinicians would find useful, it was decided to hold an additional session for the UK delegates following the closure of the main part of the meeting. The agenda for this was only recently confirmed and a copy was provided. As the decision to include an extra session had been made before the flights were booked it was appropriate to arrange the delegates' return flights so that airport transfers could begin after the close of this additional session. If it was possible for a delegate to catch a return flight that evening (Saturday, 13 April) the arrangements were made. If, however, there were no return flights to their airport of choice or logistical issues dictated that they would be travelling particularly late (such as if they would have a significant onward journey following arrival in the UK) then it was reasonable to offer an additional night's accommodation in Barcelona and arrange return travel for the next day (Sunday, 14 April). Details of the travel arrangements of each of the delegates were provided.

The decision to hold an additional UK session was made before the 'Save the date' card was sent and so it was decided to give a degree of warning that return travel from the meeting might therefore include Sunday, 14 April. Gedeon Richter offered and paid for only the minimum number of nights' accommodation in the hotel that would be required to facilitate attendance at the meeting.

Gedeon Richter provided several screenshots of the website that delegates would visit to register for the meeting and to indicate their travel plans.

Gedeon Richter stated that Esmya 5mg was currently indicated '…for pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The duration of treatment is limited to 3 months'. This indication was obtained as part of the marketing authorization which was granted largely as a result of the PEARL I and PEARL II studies. These studies used doses of 5mg and 10mg once daily and the data was referred to in the Esmya SPC. PEARL III was a placebo-controlled study to assess the benefit of a short course of progestin (or placebo) following Esmya 10mg for 12 weeks for the treatment of fibroids. These treatments were then repeated three further times. The use of repeated courses of Esmya was described in the Esmya Risk Management Plan as an

area of 'missing information' and so one key aim of PEARL III was to help to provide this information.

PANEL RULING

The Panel noted that Gedeon Richter had organised two meetings in Barcelona, one in April 2013 and the other in March 2012.

The Panel reviewed relevant requirements of the Code in relation to meetings, hospitality and sponsorship and Gedeon Richter UK's responsibility.

Clause 19.1 stated that 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 costs involved must not exceed that level which the recipients would normally adopt when paying for themselves. The supplementary information to Clause 19.1 made it clear that the provision of hospitality was limited to refreshments/subsistence, accommodation, genuine registration fees and the payment of reasonable travel costs which a company might provide to sponsor a delegate to attend a meeting. The venue must not be lavish, extravagant or deluxe and companies must not sponsor or organise entertainment such as sporting or leisure events. In determining whether a meeting was acceptable or not, consideration needed to be given to the educational programme, overall cost, facilities offered by the venue, nature of the audience, subsistence provided and the like. It should be the programme that attracted delegates and not the associated hospitality or venue. The supplementary information also stated that a useful criterion in determining whether the arrangements for any meeting were acceptable was to apply the question 'Would you and your company be willing to have these arrangements generally known?' The impression that was created by the arrangements for any meeting must always be kept in mind.

The Panel also noted the supplementary information to Clause 19.1, Meetings and Hospitality, which stated that meetings organised by pharmaceutical companies which involved UK health professionals at venues outside the UK were not necessarily unacceptable. There had, however, to be valid and cogent reasons for holding meetings at such venues. These were that most of the invitees were from outside the UK or, given the location of the relevant resource or expertise that was the object or subject matter of the meeting, it made greater logistical sense to hold the meeting outside the UK. As with meetings held in the UK, in determining whether such a meeting was acceptable or not, consideration must also be given to the educational programme, overall cost, facilities offered by the venue, nature of the audience, subsistence provided and the like. As with any meeting it should be the programme that attracted delegates and not the associated hospitality or venue.

The Panel noted that Clause 3 prohibited the promotion of a medicine prior to the grant of the marketing authorization and required that promotion was in accordance with the marketing authorization and not inconsistent with the SPC. The supplementary information to Clause 3, Marketing Authorization, stated that 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 this or any other clause.

1 Barcelona meeting April 2013

The Panel noted that the front page of the meeting invitation was headed 'Save the date!' and featured the brand imagery associated with Esmya. In that regard the Panel considered that recipients would immediately associate the meeting with Esmya. The invitation stated that the meeting was about SPRMs and ulipristal acetate for the treatment of uterine fibroids. The invitation referred to 'highly scientific and interactive sessions on new phase III clinical data evaluating the efficacy and safety of ulipristal acetate in the treatment of uterine fibroids'. The indication was included as a footnote which stated that Esmya 5mg was indicated for the pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age with a treatment duration limited to 3 months. The Panel considered that the invitation itself promoted Esmya for the treatment of uterine fibroids. Prescribing information was included on the reverse. The Panel was concerned that Gedeon Richter submitted that the invitation was not promotional. It could not be anything else given that it referred to a product and included an indication.

The Panel did not consider that the invitation promoted Esmya for an unlicensed indication. Although the invitation mentioned new phase III data it only referred to the product's use in the treatment of uterine fibroids and details of the indication were included. The Panel considered that there was no breach of Clause 3.2 and ruled accordingly. The meeting discussed the new phase III data which according to Gedeon Richter's submission included data on the 10mg dose which was not licensed. The Panel noted Gedeon Richter's submission that the SPC included some of the 10mg data. It also noted that there was no complaint in this regard about the meeting.

The invitation asked the recipient to save the 12, 13 and 14 April. According to the programme the meeting started on Friday, 12 April at 14.15 and finished at 17.30. This was followed by dinner. The agenda for 13 April ran from 09.00–12.00. There was no date of preparation on the agenda document.

The Panel was concerned that the invitation implied that the meeting would finish on 14 April. This was not so. The meeting referred to on the invitation 'International Scientific Symposium dedicated to Selective Progesterone Receptor Modulators (SPRMs) and ulipristal acetate for the treatment of uterine fibroids' finished at midday on 13 April. The Panel failed to see why a meeting arranged to finish at midday on 13 April required delegates to keep 14 April free. A symposium for UK delegates was arranged from 14.00-17.00 on 13 April. This was not mentioned

on the save the date card. The Panel did not know when the company informed the UK delegates about this additional seminar. The Panel noted Gedeon Richter's submission that the decision to hold the UK seminar was made before the save the date card had been sent. The Panel queried why the afternoon seminar was not mentioned on the invitation card.

The Panel noted that 18 of the UK delegates had stayed on in Barcelona for the night of 13 April as the finish time of the meeting (17.00) meant that either they could not catch flights back that evening or they considered the time of a possible return flight was inconvenient. One delegate considered that a possible flight at 19.20 (used by other delegates) was too late on the Saturday evening to return home because, *inter alia*, he/she had a long drive from the airport; this delegate returned instead at 20.00 on the Sunday. Two other people also decided against a possible 19.20 flight home on the Saturday and their request to stay an extra night was granted 'due to the time being close'. The Panel noted that the delegates' difficulties in getting back to the UK on the Saturday evening appeared to contradict Gedeon Richter's submission that Barcelona was chosen because of its easy travel links. Dinner was provided for those who stayed in Barcelona on the Saturday night. Sixteen delegates flew back to the UK on the Saturday evening and one delegate paid for his own accommodation for the Saturday evening. Some delegates had had three nights' accommodation paid. For a few of the delegates this was so that they could catch early flights out of the UK on 12 April. The Panel did not consider that the content of both meetings justified two or three nights' accommodation.

The Panel noted Gedeon Richter's reasons for choosing Barcelona. The speakers and delegates were mainly from European countries; the number of UK delegates (40) was the fourth largest group and the Spanish delegates formed the third largest group (42). The Panel accepted that for a European meeting many delegates would have to travel but considered the company should have made better use of the time so that no one needed to stay for two nights. The Panel was concerned about the arrangements. It queried why the meeting for UK health professionals had not started sooner than 2 hours after the end of the morning meeting and when delegates had been informed about this meeting; the afternoon session for UK delegates was referred to in the final confirmation letter to delegates. The Panel was concerned that the save the date card gave the impression that there would be scientific content on the Sunday.

This was the second year that the company had organised a meeting in Spain.

Overall, the Panel considered the arrangements were unacceptable and a breach of Clause 19.1 was ruled.

The Panel noted that Gedeon Richter acknowledged that the invitation to the meeting outside the UK had not been certified by a registered medical practitioner or a UK registered pharmacist as required by Clause 14.2 and a breach of Clause 14.2 was ruled.

The Panel noted that the invitation had been available on the events management agency website. The Panel noted Gedeon Richter's submission that this role had been passive and that there were no Internet search engine optimisation techniques applied to the website. Further it was unlikely that a health professional or a member of the public would stumble upon the invitations without being directed by other means. Health professionals would only be directed to the website if they had received a hard copy of the invitation from a Gedeon Richter representative. The Panel did not consider that in these circumstances the availability of the invitation on an events management website constituted advertising a prescription only medicine to the public as alleged. No breach of Clause 22.1 was ruled.

The Panel considered that the rulings of breaches regarding the arrangements for the meeting including the failure to certify meant that high standards had not been maintained and a breach of Clause 9.1 was ruled. The Panel considered that the arrangements brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

2 Invitation to the Barcelona meeting 2012

The Panel noted that a save the date letter had been sent in December 2011 for a meeting to be held in Barcelona on 2 and 3 March 2012. The meeting invitation was headed 'Scientific symposium dedicated to SPRMs and ulipristal acetate, Barcelona, Spain'. The agenda included presentations on Esmya and phase III data. The meeting ran from 15.15 to 18.30 on 2 March and 9.00 – 12.30 the following day.

The Panel noted that according to the Esmya SPC it was first authorized in February 2012.

The Panel noted Gedeon Richter's reasons for choosing Barcelona.

The Panel was concerned that the save the date invitation in effect promoted an unlicensed medicine. The invitation dated December 2011 referred to the product by generic name and that it was a SPRM. The preliminary programme which appeared to have been sent with the invitation included the brand name Esmya in logo format and presentations 'How is Esmya different'. The Panel considered that the both the agenda and the preliminary programme promoted an unlicensed medicine and a breach of Clause 3.1 was ruled. High standards had not been maintained and a breach of Clause 9.1 was ruled.

On balance, the Panel did not consider the circumstances warranted a ruling of a breach of Clause 2 of the Code which was reserved for use as a sign of particular censure.

During its consideration of the allegation about the invitation to the meeting in Barcelona, 2012 the Panel queried whether the content of the meeting would attract delegates rather than the venue. The programme content was on the limits of acceptability

in that the meeting, which lasted just over 6 hours, was spread over two days. The Panel was also concerned that the invitation and programme did not appear to have been certified prior to distribution. The invitation had a November 2011 date of preparation and was dated December 2011. The programme had a November 2011 date of preparation. The Panel did not accept the submission that the meeting met the supplementary information for Clause 3 in relation to the legitimate exchange of medical and scientific information during the development of a medicine. However, the complaint was about the content of the invitation not about its certification or the meeting itself and by the time of the meeting, Esmya had a marketing authorization. The Panel requested that its concerns were drawn to the company's attention.

Complaint received **6 February 2013**

Case completed **7 May 2013**

CASE AUTH/2576/2/13

ANONYMOUS GENERAL PRACTITIONER v ABBOTT

Promotion of Hidrasec including via social media

An anonymous, non-contactable general practitioner complained about the promotion of Hidrasec (racecadotril). Hidrasec, marketed by Abbott Healthcare, was indicated for the treatment of acute diarrhoea in adults and infants (older than 3 months).

The detailed response from Abbott is given below.

The complainant found advertisements for Hidrasec on Facebook and a video about how it worked on another website. The video labelled 'Hidrasec Mode of Action' appeared to be aimed at patients and the complainant was concerned as to where else this was available and how it would be used with patients.

The complainant noted that Abbott marketed Hidrasec but the advertisements appeared to have been posted by the advertising agency. The complainant considered that the public should not be able to see these advertisements and was concerned that this sort of information could lead patients to request Hidrasec inappropriately.

The Panel noted that it appeared that in response to a request from the UK based photographer who took the original shots, Abbott global agreed to supply a copy of the images used in the advertising campaign. The images were for the photographer's portfolio on his/her Facebook site. The Panel questioned whether Abbott global had, in allowing the files to be sent to the photographer, realized that the text would be included.

The Panel noted that Facebook was an open access website and was not limited to professional use. The Panel considered that there was a difference between putting examples of promotional material on an advertising agency's website, in a section clearly labelled in that regard and putting the same on a personal Facebook site. The Panel considered that placing the Hidrasec advertisements on Facebook in effect promoted a prescription only medicine to the public and encouraged members of the public to ask their health professional to prescribe it. Breaches of the Code were ruled. The Panel considered that high standards had not been maintained. A further breach of the Code was ruled. The Panel did not consider, however, that there had been a breach of Clause 2.

With regard to the mode of action video, the Panel noted that the video clip had been uploaded onto an animator's professional website. The Panel noted Abbott's submission that the uploaded version had been altered such that the only reference to Hidrasec was in the caption, 'Hidrasec "Mode of action" animation Abbott Laboratories Ltd. 2010', beneath the video clip. The Panel further noted that no record of the video as posted on the animator's website remained as Abbott had asked for it to be removed.

The Panel considered it was unfortunate that the caption to the video mentioned Hidrasec when mention of the product had been removed from the video. The Panel considered that as it had no idea of the content of the video it could not be certain that a prescription only medicine had been promoted to the public or that statements had been made which would encourage members of the public to ask their health professional to prescribe Hidrasec. Given these circumstances the Panel ruled no breach of the Code.

The complainant further complained that advertisements for Hidrasec, a new product, did not display a black triangle.

The Panel noted that the Code stated that when required by the licensing authority, all promotional material must show an inverted black triangle to denote that special reporting was required in relation to adverse reactions. It appeared that during the pre-vetting process, the licensing authority had not told Abbott that a black triangle was required. The product was added to the black triangle list in December 2012 and Abbott had amended its materials in January 2013 when the decision was confirmed. The Panel noted that Hidrasec material had not displayed the black triangle symbol for three months or so. The Panel noted that if there was a date on the material provided by the complainant it could not be read. The Panel considered that taking all the circumstances into account the complainant had not proved his/her complaint on the balance of probabilities. In addition the product had not been placed on the black triangle list until 3 months after it was first marketed. The Panel thus ruled no breach of the Code.

The complainant noted that as Hidrasec was only licensed for children over 3 months, Abbott could not claim that it 'provides rapid control for even your smallest patients'.

The Panel noted that Hidrasec was indicated, *inter alia*, for the complementary symptomatic treatment of acute diarrhea in infants aged over 3 months. The Panel noted that the claim at issue was preceded by the statement 'And because its licensed in infants older than 3 months …'. The Panel thus did not consider that the claim '... provides rapid control for even your smallest patients' was unacceptable as alleged; it was clearly within the context of infants older than 3 months and was thus not inconsistent with the particulars listed in the SPC. No breaches of the Code were ruled.

An anonymous, non-contactable general practitioner complained about the promotion of Hidrasec (racecadotril) and drew particular attention to material available to the public via Facebook and the Internet. Hidrasec 100mg capsules were indicated for the symptomatic treatment of acute diarrhoea in adults when causal treatment was not possible. A granular paediatric formulation was indicated as complementary oral rehydration therapy in infants (older than 3 months) with acute diarrhoea. Hidrasec was marketed by Abbott Healthcare Products Limited.

When writing to Abbott, the Authority asked it to respond in relation to Clauses 2, 3.2, 4.11, 7.2, 9.1, 22.1 and 22.2 of the Code.

1 Advertising on Facebook and the Internet

COMPLAINT

The complainant stated that whilst searching the Internet for information on Hidrasec he/she found advertisements for it on Facebook and a video about how it worked on another website. The video labelled 'Hidrasec Mode of Action' appeared to be aimed at patients and the complainant was concerned as to where else this was available and how it would be used with patients. The complainant provided links to the relevant Facebook page and Internet page.

The complainant noted that Abbott marketed Hidrasec but it appeared that the advertisements had been posted by the advertising agency. The complainant considered that it was wrong for the public to be able to see these advertisements for a prescription only medicine. The complainant was concerned that this sort of information could lead to patients requesting this product inappropriately. This was of particular concern to the complainant as Hidrasec had not been recommended for use by the Scottish Medicines Consortium (SMC). Although the complainant was based in England, he/she highly valued these assessments of new products and tended to follow their guidance.

RESPONSE

Abbott submitted that it became aware of the Hidrasec advertisements on Facebook on 8 November 2012 when a UK representative reported the matter to the UK Abbott affiliate. The advertisements corresponded to those developed by Abbott's global marketing team based in Basel, Switzerland. It was evident that the advertisements on Facebook had been changed from the original global versions as the majority of the footer text had been removed, however, they could be identified as originating from the global marketing team's materials and could be distinguished from UK specific advertisements by, *inter alia* the spelling of 'diarrhoea' (spelt diarrhea in the global material). For comparison, Abbott provided copies of the approved UK Hidrasec advertisements.

The Facebook site referred to by the complainant was that of the photographer and his/her photographic agency who worked on the photo shoot for the global Hidrasec campaign on behalf of the advertising agency. The site content concerned the professional activities of the agencies/photographer, including many examples of his/her work and technical considerations relating to his/her work. The images from the Hidrasec campaign had been provided with permission from Abbott global. There was never any intention behind this decision to promote Hidrasec to the public, the intention was only to allow the photographer to use the images he/she shot to advertise his/her work. The material was not intended for the UK audience.

Abbott stated that the UK company had a separate contract with its advertising agency to cover the development of UK specific advertisements. This agreement contained sections on intellectual property rights and advertising outside the territory. The UK contract referred separately to materials created as part of the proposal (for the exclusive use of Abbott) and photographic images (the ownership of photographic images, film and animation work was not assigned and was subject to licence agreements). The UK advertisements were therefore for the exclusive use of Abbott and there had been no subsequent permission granted by Abbott to allow use of the UK specific advertisements. Abbott submitted that it had not found any of its UK advertisements on the Internet.

Abbott stated that although it was clear that the images originated from its global team and no permission was granted for the purposes of advertising an Abbott product, Abbott considered it was good practice to telephone its advertising agency on 9 November, 2012 to ask for further information on how these materials might have been disseminated following the permission granted and request the immediate removal of the Hidrasec images from the Internet. The advertising agency immediately contacted the photographer's agent to request that he/she removed all images from Facebook as well as any other websites as soon as possible. The advertising agency confirmed its actions in emails dated 9 November.

Abbott stated that it commenced an investigation into the circumstances of both the advertisements and video appearing on the Internet and again contacted its advertising agency on 14 November to seek reassurances that materials had been removed. On 23 November its advertising agency again confirmed that the photographer's agent had removed the remaining advertising images.

Abbott did not consider that there was any attempt or intention on its part to advertise to the public. The photographer placed materials on his/her website to advertise his/her own work and no permissions were given by Abbott in the UK to place UK approved advertising on the Internet. As a result Abbott did not consider that there had been a breach of the Code. Furthermore the presence of the global advertisements not intended for a UK audience on the Internet fell outside the scope of the Code as outlined in Clause 1. Notwithstanding that there had been no breach of the Code, Abbott had taken all reasonable steps to have any images removed

from the Internet and also retrained relevant UK and global staff.

Abbott submitted that the mode of action video referred to by the complainant was also developed for the Abbott global marketing team. A screenshot corresponding with the image of the video clip on the website referenced was provided.

The video did not refer to Abbott nor was there any reference to Hidrasec or the generic name either verbally or in print as part of the video clip. The animated clip showed activities in the gut before and once diarrhoea occurred and a factual commentary to accompany it. In the commentary there was no reference to Hidrasec or racecadotril. The only reference to Hidrasec was in the caption beneath the video clip 'Hidrasec "Mode of action" animation Abbott Laboratories Ltd 2010'. The reference to 'Abbott Laboratories Ltd 2010' demonstrated that the video was produced under the global agreement and predated any UK marketing activities for the medicine.

The Internet site in question was that of the animation company which produced the video; the site detailed only the professional activities of the animation company and contained many examples of its work. Abbott stated that it had not received any request or other correspondence from its advertising agency or the animation company regarding the use of the video.

Hidrasec was licensed by the Medicines and Healthcare Products Regulatory Agency (MHRA) in September 2011 and it was commercialized in October 2012 and hence could be promoted in the UK regardless of the recent SMC decision not to recommend it.

As a result it appeared that a non-promotional video produced for the Abbott global campaign was placed on a professional Internet site by the animation company to display its work. Abbott thus did not consider that there had been a breach of the Code with regard to the promotion of Hidrasec to the public. Furthermore, the presence of global non-promotional videos not intended for a UK audience on the Internet fell outside the scope of the Code as outlined in Clause 1. However Abbott again considered it appropriate to ask for this material to be removed and had also retrained its staff as outlined above.

In response to a request for a copy of the mode of action video, Abbott submitted that the video referred to by the complainant was not the UK mechanism of action video. Abbott submitted that as this was a third party global altered version not intended for advertising the product but uploaded onto an animator's professional Internet site in order to display its work, and that as Abbott had asked for the link to be removed, it had no copies of the video to provide.

In response to a further request for more information, Abbott stated that Abbott's advertising agency, the photographer and the animation company were all based in the UK but all had an international client base with outputs shown globally. In addition the photographer was of international acclaim and had agents representing him/her in various countries around the world.

PANEL RULING

The Panel noted that it appeared that in response to a request from the photographer, Abbott global had agreed to supply a copy of the images used in the advertising campaign. The images were for the photographer's portfolio on his/her Facebook site. The photographer was based in the UK and so in that regard the Panel considered that the matter came within the scope of the Code. The Panel questioned the need for the images to be supplied complete with text and queried whether, in allowing the files to be sent to the photographer, Abbott global had realized that the text would be included and ascertained exactly what the photographer intended to do with the files.

The Panel understood that creative agencies and individuals would want to be able to show examples of their work. However pharmaceutical companies had to ensure that by facilitating such use, prescription only medicines were not advertised to the public. The structure of a website, the description of the materials and their content would be important factors.

The Panel noted Abbott's submission that the materials were from Abbott global and not Abbott UK and predated the promotion of Hidrasec in the UK.

It was a well established principle that UK pharmaceutical companies were responsible for the activities of overseas affiliates if such activities related to UK health professionals or were carried out in the UK.

The Panel noted that Facebook was an open access website and was not limited to professional use. The Panel considered that there was a difference between putting examples of pharmaceutical promotional material on an advertising agency's website, in a section clearly labelled in that regard and putting the same on a personal Facebook site. The Panel considered that placing the Hidrasec advertisements on Facebook in effect promoted a prescription only medicine to the public. A breach of Clause 22.1 was ruled. The Panel considered that statements had thus been made in a public forum which would encourage members of the public to ask their health professional to prescribe Hidrasec. A breach of Clause 22.2 was ruled.

The Panel noted its rulings above and considered that high standards had not been maintained. A breach of Clause 9.1 was ruled. The Panel did not consider, however, that there had been a breach of Clause 2. Such a ruling was the sign of particular censure and reserved for such. No breach of Clause 2 was ruled.

With regard to the mode of action video, the Panel noted that the video clip had been uploaded onto an animator's professional website. The Panel

noted Abbott's submission that the video had been developed for the global marketing team and that the version uploaded onto the animator's website had been altered to delete references to Hidrasec or racecadotril. The only reference to Hidrasec was in the caption beneath the video clip which read 'Hidrasec "Mode of action" animation Abbott Laboratories Ltd. 2010'. The Panel further noted that no record of the video as posted on the animator's website remained as Abbott had asked for it to be removed. The link to the video, provided by the complainant, no longer worked.

The Panel considered it was unfortunate that the caption to the video mentioned Hidrasec when mention of the product had been removed from the video. The Panel considered that as it had no idea of the content of the video it could not be certain that a prescription only medicine had been promoted to the public or that statements had been made which would encourage members of the public to ask their health professional to prescribe Hidrasec. Given these circumstances the Panel ruled no breach of Clause 22.1 and 22.2.

2 Absence of the inverted black triangle symbol

COMPLAINT

The complainant was also concerned that as a new product, Hidrasec should display a black triangle. The complainant had seen the same advertisements in medical journals and they did not show this. Surely this was a safety issue? The complainant stated that a copy of an advertisement from the journal 'Guidelines' was provided.

RESPONSE

Abbott noted that Hidrasec 10mg granules, 30mg granules and 100mg capsules were granted a UK marketing authorization in September 2011 with no requirement for an inclusion of a black triangle.

Abbott began to market Hidrasec in October 2012. All Hidrasec materials were sent to the MHRA for pre-vetting prior to the launch of the product. The MHRA did not request the addition of a black triangle. Abbott stated that it had no reason to suspect that Hidrasec would be a black triangle product as it had been licensed for over 10 years across Europe and the company had been informed by the MHRA to remove the black triangle from several of its other products as the black triangle scheme was to be phased out in anticipation of the new EU products for extensive monitoring list. Also the grant letter issued by the MHRA did not include any requirements for a black triangle to be added.

Therefore the materials used at this stage of the campaign were the pre-vetted MHRA materials and did not contain any black triangle warnings.

Abbott noted the complainant's reference to an advertisement from 'Guidelines' but as a copy had not been provided, the company could not comment on this advertisement.

Abbott first noticed that the MHRA had assigned a black triangle in the MHRA black triangle list – December 2012. Abbott immediately contacted the MHRA for clarification as it had not been informed of this and the list did not state that this was a new addition for that month. On 21 December the MHRA confirmed that Hidrasec had been added to the list but in error it was not flagged as a new edition. An urgent company communication was sent out to the field force (and head office) to quarantine all Hidrasec materials with clear instructions that materials should not be used (21 December). Agencies were also instructed to halt or remove any Hidrasec advertising.

On the first week of January Abbott was informed that the MHRA would review its decision. Abbott received a decision from the MHRA on 18 January that the black triangle would remain.

An immediate withdrawal and destruction of Hidrasec material was initiated. Materials had since been reprinted and recertified.

Journals were notified on 24 January 2013.

PANEL RULING

The Panel noted that the complainant had provided a copy of what appeared to be two advertisements. One featured a child kneeling and playing with a radio-controlled flying toy and another featured a child walking with a pull-along toy. It was not clear from these pages whether these were the advertisements published in Guidelines or not. They had website addresses. The Panel had no idea of the date of these advertisements.

Abbott stated that the complainant had not provided an advertisement. As the complainant was anonymous and non-contactable it was not possible to follow up on this.

The Panel noted that in correspondence with Abbott, the MHRA had stated that Hidrasec was added to the black triangle list in December 2012 when the agency became aware that the medicine was being marketed. The MHRA explained that products were only added to the black triangle list once the product was marketed and not when the marketing authorization was granted. The Panel noted, however, that the Hidrasec materials had been pre-vetted without any reference by the MHRA to the requirement to add a black triangle. Abbott had assumed that as Hidrasec had been available for over 10 years in Europe, it would not be subject to special reporting in relation to adverse reactions. The Panel noted Abbott's submission that once it was aware of the situation it had acted quickly to withdraw and destroy Hidrasec material without the triangle and reprint and issue new material.

The Panel noted that Clause 4.11 of the Code stated that when required by the licensing authority, all promotional material must show an inverted black triangle to denote that special reporting was required in relation to adverse reactions. It appeared that during the pre-vetting process,

the licensing authority had not told Abbott that a black triangle was required. The product was added to the black triangle list in December 2012 and Abbott had amended its materials in January 2013 when the decision was confirmed. The Panel noted that Hidrasec material had not displayed the black triangle symbol for three months or so. The Panel noted that if there was a date on the material provided by the complainant it could not be read. The Panel considered that taking all the circumstances into account the complainant had not proved his/her complaint on the balance of probabilities. In addition the product had not been placed on the black triangle list until 3 months after it was first marketed. The Panel thus ruled no breach of Clause 4.11.

3 Claim 'provides rapid control for even your smallest patients'

COMPLAINT

The complainant noted that as Hidrasec was only licensed for children over 3 months, Abbott could not claim that it 'provides rapid control for even your smallest patients'.

RESPONSE

Abbott noted that the claim at issue did not exist in isolation, but followed 'because it's licensed in infants older than 3 months' as shown below:

> 'Hidrasec specifically targets the uncontrolled secretory processes that underlie acute diarrhoea, reducing stool output and diarrhoea duration. **And because it's licensed in infants older than 3 months, Hidrasec, together with oral rehydration solution, provides rapid control for even your smallest patients'** (emphasis added).

Abbott submitted that Hidrasec was the only licensed anti-diarrhoeal in infants aged 3 months and above. Other anti-diarrhoeals were licensed for use in children aged 4 years and above. As the advertisement made it clear that the product was licensed from 3 months of age Abbott considered that this statement could be justified. Although Abbott acknowledged that MHRA pre-vetting of material did not equate to an automatic approval it noted that this advertisement had been pre-vetted by the MHRA and the statement was not disputed.

Abbott assured the complainant that it was committed to patient safety and strove to ensure appropriate messaging be aligned to its products.

PANEL RULING

The Panel noted that Section 4.1 of the Hidrasec summary of product characteristics (SPC) stated that the medicine was indicated, *inter alia*, for the complementary symptomatic treatment of acute diarrhea in infants aged over 3 months. The Panel noted that the claim at issue was preceded by the statement 'And because its licensed in infants older than 3 months...'. The Panel thus did not consider that the claim '...provides rapid control for even your smallest patients' was unacceptable as alleged; it was clearly within the context of infants older than 3 months and was thus not inconsistent with the particulars listed in the SPC. No breach of Clause 3.2 was ruled. The Panel did not consider that the claim was misleading; no breach of Clause 7.2 was ruled.

Complaint received **6 February 2013**

Case completed **17 April 2013**

CASE AUTH/2580/2/13

EX-EMPLOYEE v GEDEON RICHTER

Meeting invitation

An ex-employee complained about an invitation to a meeting in Manchester, 6 March 2013, entitled 'Selective Progesterone Receptor Modulators (SPRMs) and a new treatment for uterine fibroids'. The invitation stated that the meeting was supported by an unrestricted educational grant from Gedeon Richter. Gedeon Richter marketed Esmya (ulipristal acetate) which was a synthetic SPRM indicated for the pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age.

The complainant noted that the invitation, which referred to SPRMs and a new treatment for uterine fibroids, was publicly available on Gedeon Richter's events company's website. One presentation would cover 'Current treatment options for patients with moderate to severe uterine fibroids' and 'Patient & surgical experience post treatment of ulipristal acetate'. The complainant stated that the invitation would be considered promotional as it contained Esmya branding and an indication. The complainant alleged that prescribing information should have been included.

Prescription only medicines should not be promoted to the public. The complainant noted that the invitation contained the name of the medicine, its indication, had promotional branding (imagery) and was freely accessible to the public.

The detailed response from Gedeon Richter is given below.

The Panel noted that the front page of the invitation featured the brand imagery associated with Esmya. Recipients would immediately associate the meeting with Esmya. According to the invitation the meeting was about SPRMs and a new treatment for uterine fibroids. The invitation referred to a presentation which would cover 'Current treatment options for patients with moderated to severe uterine fibroids' and about 'Patient & surgical experience post treatment of ulipristal acetate'. The Panel considered that the invitation promoted Esmya. As no prescribing information was included a breach of the Code was ruled. This ruling was accepted by Gedeon Richter.

The Panel noted that the invitation had been available on the events company's website. The Panel noted Gedeon Richter's submission that the role of the events company had been entirely passive and that it had facilitated online registration to the meeting. Further, only health professionals who had been invited to the meeting would have known about the website and that no branding or imagery had been used with the public. The Panel did not consider that in these circumstances the availability of the invitation on an events company's website constituted advertising a prescription only medicine to the public as alleged. No breach of the Code was ruled. This ruling was appealed by the complainant.

The Panel noted its rulings above and did not consider the circumstances warranted a ruling of a breach of Clause 2. No breach of Clause 2 was ruled. This ruling was appealed by the complainant.

The Appeal Board noted that the two tweets provided by the complainant on appeal, did not refer to the meeting at issue.

The Appeal Board noted Gedeon Richter's submission to the Panel that the invitation to the Manchester meeting had been available on the events company's website and only health professionals invited to the meeting would have known of its whereabouts. The Appeal Board noted the tweets from events company about other meetings but considered the complainant had not provided any evidence to show that details of the Manchester meeting had been tweeted. The Appeal Board thus did not consider that, with regard to the meeting at issue, a prescription only medicine had been promoted to the public as alleged. The Appeal Board upheld the Panel's rulings of no breach of the Code including Clause 2. The appeal was thus unsuccessful.

During its consideration of this case, the Appeal Board was extremely concerned that Gedeon Richter had provided the Panel with inaccurate information about the role of the events company. Although no evidence had been produced to show that the events company tweeted information about the meeting at issue, it was clear that it had tweeted details of other meetings to include the name of a medicine and its indication. The events company was thus not entirely passive in relation to meetings and invitations as submitted.

An ex-employee of Preglem UK (a wholly owned subsidiary of Gedeon Richter) complained about an invitation (ref GR-ADV 13/0010) to a meeting in Manchester, 6 March 2013, entitled 'Selective Progesterone Receptor Modulators (SPRMs) and a new treatment for uterine fibroids'. The invitation stated that the meeting was supported by an unrestricted educational grant from Gedeon Richter. Gedeon Richter marketed Esmya (ulipristal acetate).

Esmya 5mg was indicated for the pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The duration of treatment was limited to 3 months. The summary of product characteristics (SPC) stated that the marketing authorization holder was Gedeon Richter plc Budapest. Esmya was an orally active synthetic SPRM and was first licensed in February 2012.

COMPLAINT

The complainant noted that the invitation was publicly available on an events management company website. The complainant further noted that the invitation referred to SPRMs and a new treatment for uterine fibroids. On page 2 of the invitation, which detailed the presentations to be given, the complainant noted that one of the speakers would talk about 'Current treatment options for patients with moderate to severe uterine fibroids' and 'Patient & surgical experience post treatment of ulipristal acetate'.

The complainant stated that the invitation would be considered promotional under Clause 1.2 as the meeting was sponsored by a pharmaceutical company and contained branding (imagery) particular to Esmya. As noted above, the name of the medicine and its indication were also stated.

The complainant alleged that under Clause 4.1 prescribing information should have been included on the invitation.

The complainant noted that under Clause 22.1, a prescription only medicine should not be promoted to the public. The complainant submitted that the invitation contained the name of the medicine, its indication, had promotional branding (imagery) and was freely accessible to the public.

When writing to Gedeon Richter the Authority asked it to respond in relation to Clause 2, in addition to Clauses 4.1 and 22.2 cited by the complainant.

RESPONSE

Gedeon Richter noted that Clause 4.1 stated 'The prescribing information listed in Clause 4.2 must be provided in a clear and legible manner in all promotional material for a medicine except for abbreviated advertisements (see Clause 5)'. The invitation at issue was to a scientific symposium about uterine fibroids entitled 'Selective Progesterone Receptor Modulators (SPRMs) and a new treatment for uterine fibroids'. There was no mention of ulipristal acetate or Esmya (the brand name) on the front of the invitation. On the back of the invitation ulipristal acetate was only mentioned in the context of 'Patient & surgical experience post treatment of ulipristal acetate'. Gedeon Richter submitted that there were clearly no claims made or elements of the therapeutic indication mentioned in the invitation. Gedeon Richter thus did not consider that the invitation promoted ulipristal acetate; the invitation represented an opportunity for clinicians to engage in appropriate scientific discussion about the therapies available for use in the overall treatment of uterine fibroids. Gedeon Richter did not consider that the invitation promoted a medicine and therefore there was no requirement to include the prescribing information. As such the company denied a breach of Clause 4.1.

The invitation to the symposium was available on the website for the events management company. The events management company acted in an entirely passive role on behalf of Gedeon Richter to facilitate the online registration of invitees to meetings that the company had developed. The events management company did not engage in active promotion, nor did it employ search engine optimisation techniques and so to find the site would require very specific knowledge such as having been given a hard copy of an invitation on which the registration website details could be found. Without this knowledge, which was not publicly available, it was extraordinarily unlikely that a member of the public could gain access to the invitation. The complainant could find the website and invitation as he/she had been previously privy to this specific information. The only people who knew about the location of the invitation and registration details for the meeting were health professionals who had been given an invitation following interaction with a Gedeon Richter representative. Gedeon Richter stated that it, and the many other pharmaceutical companies that used the services of the events management company, considered the entirely passive nature of the events management company in relation to meetings and invitations was sufficient to ensure that members of the public were not exposed to information that might be construed as being promotional. As such the company denied a breach of Clause 22.1.

Gedeon Richter stated that given the above it strongly considered that it had not brought discredit upon, or reduced confidence in, the pharmaceutical industry and it thus strongly refuted any suggestion that it had breached Clause 2.

In response to a request for further information, Gedeon Richter submitted that the invitations to the meeting in Manchester were distributed to local gynaecologists with an interest in the treatment of uterine fibroids. The invitations were distributed by the field-based key account managers either as a hard copy or by email.

Although the approval certificate could imply that the email could be sent directly by the events management company, the statement (assumed to be 'hand-out or via emial by KAMS/[events management company']) was intended to refer to the fact that the layout and artwork of the email was created by the events management company but it was to be sent by the key account managers. The events management company did not send out the meeting invitation directly.

Gedeon Richter provided a pad of tear-off patient information sheets designed to support clinicians treating uterine fibroids. The text provided brief information and instructions for the patient and an image of the female reproductive system which was intended to facilitate discussion between the clinician and the patient. This was the only material that was for use by or with the patient; there was no branding or imagery and the general appearance was entirely functional.

PANEL RULING

The Panel noted that the front page of the meeting invitation featured the brand imagery associated with Esmya. In that regard the Panel considered that

recipients would immediately associate the meeting with Esmya. The invitation stated that the meeting was about SPRMs and a new treatment for uterine fibroids. The second page of the invitation referred to a presentation which would cover 'Current treatment options for patients with moderated to severe uterine fibroids' and about 'Patient & surgical experience post treatment of ulipristal acetate'. The Panel considered that the invitation itself promoted Esmya for the treatment of uterine fibroids and in that regard should have incorporated the prescribing information for the medicine. As no prescribing information was included a breach of Clause 4.1 was ruled. This ruling was accepted by Gedeon Richter.

The Panel noted that the invitation had been available on the events management company website. The events management company was an events management agency. The Panel noted Gedeon Richter's submission that the events management company's role had been entirely passive and that it had acted to facilitate online registration of invitees to the meeting. Further, only health professionals who had been invited to the meeting would have known about the website and that no branding or imagery had been used with the public. The Panel did not consider that in these circumstances the availability of the invitation on an events management company website constituted advertising a prescription only medicine to the public as alleged. No breach of Clause 22.1 was ruled. This ruling was appealed by the complainant.

The Panel noted its rulings above and did not consider the circumstances warranted a ruling of a breach of Clause 2 which was reserved as a sign of particular censure. No breach of Clause 2 was ruled. This ruling was appealed by the complainant.

During its consideration of this case, the Panel was concerned that the invitation stated that the meeting was 'Supported by an unrestricted educational grant by the Women's Health Division of Gedeon Richter (UK) Ltd' which it considered might give a misleading impression that Gedeon Richter had given an arm's length grant to a third party for it to organise the meeting. This was not so. The meeting was a Gedeon Richter meeting and this should have been made clear. The Panel was further concerned that the date of first authorization of Esmya was 23 February 2012. The invitation was dated February 2013 and referred to 'a new treatment for uterine fibroids'. The Panel assumed that the new treatment was Esmya but noted that Clause 7.11 stated that 'new' must not be used to describe any products which had been generally available for more than twelve months in the UK. The Panel thus queried whether the invitation met the requirements of that clause.

APPEAL FROM THE COMPLAINANT

The complainant appealed the Panel's ruling of no breach of Clauses 2 and 22.1.

The complainant alleged that Gedeon Richter's submission that the events management company had acted in an entirely passive role on its behalf seemed untrue and that the company had misled the Panel on this assessment. The events management company had not only produced the promotional items but it had also actively promoted the meeting on its twitter page. A tweet on 9 November stated 'Register for the event "Sharing surgical experience after the use of ulipristal acetate in fibroid patients"'. The complainant noted the inclusion of the name of the medicine and its use. There was a similar message on 22 of November to register for an event. These twitter messages threw some light on the relationship between Gedeon Richter marketing and the events management company and how the events management company played an active role in marketing the medicine.

The complainant requested that the Appeal Board enquired about the approval of these twitter messages which the complainant was sure the company would be quick to deny.

COMMENTS FROM GEDEON RICHTER

Gedeon Richter submitted that it had been entirely unaware of, and in no way requested or sanctioned the tweet on the events management company twitter feed. Gedeon Richter's discussion with the events management company as to the nature of its activities relating to meetings it sponsored described that its expectations were that the events management company would passively facilitate registration. It appeared that these expectations were not sufficiently transmitted through the management company staff with the outcome being that this tweet appeared on its twitter feed at the time that registration system could be accessed.

Gedeon Richter stressed that it did not request, permit or otherwise agree to the meeting being advertised in this manner and, despite the complainant's view, it did not seek to mislead the Panel. Gedeon Richter understood that it was responsible for the actions of its service providers and that in this case it was clear that a tweet was released into the public domain which mentioned the name of the product and other information about the licensed indication which could therefore be perceived as being promotional.

Gedeon Richter noted that as the current number of followers of the events management company on its twitter feed was very low it was unlikely that many people saw this tweet, particularly as it was broadcast at 1.37am. But the company accepted that the tweet could potentially represent a breach of the Code. Gedeon Richter submitted that given its belief that the likelihood that the audience for the tweet was low and that this specific action was unlikely to bring discredit upon, or reduce confidence, in the pharmaceutical industry, this did not represent a breach of Clause 2 of the Code.

Gedeon Richter submitted that the nature of the complaint and the complainant led it to believe that it knew the identity of the complainant. Although the complainant remained anonymous and the nature of the complaint was not material to the case in hand, Gedeon Richter considered that the complaint had been initiated through motives other

than a desire to uphold the letter and spirit of the Code. If the company was correct in its assumption as to the identity of the complainant then it was unable to explain why someone who purported to be a defender of the Code failed to apply the same level of scrutiny to the materials at hand when they were employed. Gedeon Richter surmised that the complainant may have known about the tweet whilst still employed by the company and so it queried why nothing was done about it at the time. Gedeon Richter felt slightly ambushed by the complainant in this regard.

Despite Gedeon Richter's assumptions and beliefs surrounding the case it also recognised that there were remedial actions that it could and should have taken. Gedeon Richter noted that it had initiated a thorough and comprehensive review and update of its promotional activities and it would also review its ongoing working arrangements with the events management company, with particular emphasis on its behaviours relating to future events.

FINAL COMMENTS FROM THE COMPLAINANT

The complainant noted that as expected, Gedeon Richter claimed that it had no knowledge of the twitter messages that the events management company had sent, and that the events management company twitter account had very few followers. The complainant noted that twitter accounts were by default public and visible to anyone with or without a twitter account. Twitter users were aware of this public display hence many companies chose this form of marketing.

The complainant noted that with the provision of free alert tools provided by various search engines, one need not look for the website or twitter messages. The public and patients who looked for new therapies or new medicines could set these alerts to learn about what was available and whenever something was new, an email was automatically sent with the link. This was how the complainant knew about the events management company tweets as the alert had picked up several recent new tweets about the medicines. There was a recent meeting held in Barcelona specifically on this medicine. There were various other tweets available; however it would not be appropriate to provide additional material at this point.

The complainant alleged that the participation of the events management company on twitter was looked at within the alerts when Gedeon Richter claimed that it had instructed the events management company to be a passive participant. There was no element of 'ambush' as claimed by Gedeon Richter.

APPEAL BOARD RULING

The Appeal Board noted that the two tweets from the events management company, cited by the complainant, did not refer to the meeting at issue in this case ie 'Selective Progesterone Receptor Modulators (SPRMs) and a new treatment for uterine fibroids' held in Manchester on 6 March 2013. The tweet of 9 November stated 'Register for the event "Sharing surgical experience after the use of ulipristal acetate in fibroid patients"'. The tweet of 22 November stated 'Places available at the Nottingham symposium on uterine fibroids'.

The Appeal Board noted Gedeon Richter's submission to the Panel that the invitation to the Manchester meeting had been available on the events management company website and only health professionals invited to the meeting would have known of its whereabouts. The Appeal Board noted tweets from the events management company about other meetings but considered the complainant had not provided any evidence to show that details of the Manchester meeting had been tweeted by the events management company. The Appeal Board thus did not consider that, with regard to the meeting at issue, a prescription only medicine had been promoted to the public as alleged. The Appeal Board upheld the Panel's ruling of no breach of Clause 22.1. The Appeal Board consequently also upheld the Panel's ruling of no breach of Clause 2. The appeal was thus unsuccessful.

During its consideration of this case, the Appeal Board was extremely concerned that Gedeon Richter had provided the Panel with inaccurate information about the role of the events management company. Although no evidence had been produced to show that the events management company tweeted information about the meeting at issue, it was clear that it had tweeted details of other meetings to include the name of a medicine and its indication. The events management company was thus not entirely passive in relation to meetings and invitations as submitted. In that regard the Appeal Board noted that companies such as the events management company were usually engaged to maximise attendance at meetings and so were unlikely to be passive.

The Appeal Board further noted that the Authority had issued guidance on digital communications to include the use of social media. Companies must know and control what third parties acting on their behalf might do in that regard.

Complaint received **20 February 2013**

Case completed **30 May 2013**

CASE AUTH/2581/2/13

BOEHRINGER INGELHEIM AND LILLY v MERCK SHARP & DOHME

Promotion of Januvia

Boehringer Ingelheim and Lilly complained that a Januvia (sitagliptin) leavepiece issued by Merck Sharp and Dohme raised doubts about the efficacy of their medicine Trajenta (linagliptin). Januvia and Trajenta were both indicated for the treatment of type 2 diabetes.

The complainants noted a bar chart which depicted glycaemic data adapted from Gallwitz *et al* (2012), a non-inferiority study to assess the long-term efficacy and safety of linagliptin vs glimepiride (a sulphonylurea). The study demonstrated that linagliptin was non-inferior to glimepiride with regard to glycaemic control. Secondary endpoints of hypoglycaemic events and change in bodyweight were in favour of linagliptin and were key considerations for clinicians.

The complainants alleged that the bar chart did not allow the reader to form a full and balanced opinion of the efficacy of linagliptin vs glimepiride as there was no reference to the secondary endpoints. The complainants further noted that on the page following the bar chart there were several claims for Januvia. The complainants alleged that the bar chart, followed immediately by claims for Januvia would lead the reader to draw indirect comparisons with linagliptin.

The detailed response from Merck Sharp & Dohme is given below.

The Panel noted that the leavepiece was used proactively to distinguish Januvia from linagliptin in those areas where linagliptin represented a significant commercial challenge. Merck Sharp & Dohme stated that the leavepiece was not intended as a comparison between linagliptin and sulphonylurea, but rather linagliptin and sitagliptin. Given the purpose of the leavepiece, the Panel did not consider that the omission of the hypoglycaemia and body weight results from Gallwitz *et al* was unacceptable. No breach of the Code was ruled.

The Panel noted that the only efficacy data presented regarding linagliptin was the bar chart depicting the results of Gallwitz *et al* which showed that at one year linagliptin lowered HbA_{1c} by 0.38% and at two years by 0.16%. The Panel noted that the two year figure was within the non-inferiority margin of 0.35%. Given the purpose of the leavepiece the Panel queried whether Gallwitz *et al*, in isolation, gave an accurate and balanced overview of the efficacy of linagliptin. Studies (other than Gallwitz *et al*) cited in the Trajenta (linagliptin) summary of product characteristics (SPC) referred to reductions in HbA_{1c} compared to placebo ranging from -0.72% after 52 weeks to -0.57% at 18 weeks. The Panel acknowledged that the results from trials cited in the SPC could not be directly compared but nonetheless such data suggested that the reduction in HbA_{1c} that could be expected from the medicine might be more in the region of -0.5-0.6% as opposed to the -0.38% and -0.16% reported by Gallwitz *et al*. The Panel did not consider that the use of Gallwitz *et al*, in isolation, provided a fair and balanced overview of the efficacy of linagliptin. The Panel considered that the bar chart would unfairly raise doubts about the clinical value and efficacy of linagliptin as alleged and was misleading in that regard. Breaches of the Code were ruled.

The Panel noted that the page of the leavepiece which featured the bar chart was followed by a page listing the key selling points of Januvia, one of which was 'Significant HbA_{1c} reductions'. In the Panel's view, given the stated purpose of the leavepiece, the reader would draw an indirect comparison between this claim and the very small reductions in HbA_{1c} depicted for linagliptin in the bar chart on the previous page. The Panel noted its comments above and considered that the comparison between linagliptin and Januvia was thus misleading. A breach of the Code was ruled.

The Panel noted its rulings above and considered that high standards had not been maintained. A breach of the Code was ruled.

Boehringer Ingelheim Limited and Eli Lilly and Company Limited complained about the promotion of Januvia (sitagliptin) by Merck Sharp and Dohme Limited. Januvia was a dipeptidyl peptidase 4 (DPP-4) inhibitor. It was indicated for adult type 2 diabetics to improve glycaemic control as monotherapy, dual combination therapy and triple combination therapy in certain patients. Boehringer Ingelheim and Lilly marketed Trajenta (linagliptin), also a DPP-4 inhibitor with similar indications to Januvia.

The material at issue was a leavepiece (ref DIAB-1061227) which Boehringer Ingelheim and Lilly alleged had been in circulation in its current form since November 2012. The first version of the leavepiece appeared in May 2012 and inter-company dialogue, which started in August 2012, led to minor alterations but these fell short of reaching a compromise agreeable to all. The leavepiece was headed 'Januvia – for type 2 diabetes patients uncontrolled on metformin alone'.

The page at issue, page 3, was headed 'Linagliptin vs an SU [sulphonyl urea] (glimepiride) both on top of metformin' followed by the subheading 'With a pre-

specified non-inferiority margin of 0.35%, linagliptin demonstrated non-inferiority vs an SU in reducing HbA_{1c}'. The page featured a bar chart headed 'Mean HbA_{1c} reductions from baseline at 52 weeks and 104 weeks when adding glimepiride 1-4mg or linagliptin 5mg to prior metformin therapy'. The bar chart showed that at 52 weeks the reductions in HbA_{1c} observed with glimepiride and linagliptin were 0.6% and 0.38% respectively. At 104 weeks the reductions were 0.36% and 0.16% respectively.

COMPLAINT

Boehringer Ingelheim and Lilly submitted that the leavepiece was a linagliptin rebuttal/objection-handler. The companies were unclear about the nature of the rebuttal/objections being handled by the leavepiece but were clear that its principal purpose was to raise doubts in the reader's mind about the efficacy of linagliptin and to imply the added benefits of Januvia through the use of indirect comparisons ie in the absence of head-to-head data upon which to make such a comparison. This view was consistent with feedback from both companies' field forces and from clinicians. Boehringer Ingelheim and Lilly alleged breaches of Clauses 7.2, 7.3, and 9.1.

Page 3 of the document included glycaemic data adapted from Gallwitz *et al* (2012) presented as a bar chart. The companies stated that the objective of this non-inferiority study was to assess the long-term efficacy and safety of linagliptin compared with the sulphonylurea glimepiride. The primary end point was change in HbA_{1c} at 2 years; the two main secondary endpoints were hypoglycaemic events and change in body weight.

The study demonstrated that linagliptin was non-inferior to glimepiride with regard to glycaemic control. An adapted representation of the glycaemic endpoints between linagliptin and glimepiride was presented as a bar chart showing the HbA_{1c} changes at 1 and 2 years. The former was an additional secondary endpoint.

The companies alleged that the bar chart did not present the data in a clear, fair, and balanced manner in breach of Clause 7.8 which required that graphs and tables were not included unless they were relevant to the claims or comparisons made. The companies submitted that as the leavepiece was a linagliptin rebuttal/objection-handler it stood to reason that it would be unfairly used to question the clinical value of linagliptin.

Boehringer Ingelheim and Lilly submitted that the data presented did not allow the reader to form a full and balanced opinion of the efficacy and safety of linagliptin compared with glimepiride. In addition to the glycaemic endpoints the study also demonstrated significant benefits of linagliptin treatment vs glimepiride. The key secondary endpoints revealed a 5-fold reduction in hypoglycaemic events and a weight differential of -2.7kg in favour of linagliptin. Reduction in risk of hypoglycaemia and weight gain were key considerations for clinicians treating type 2 diabetes. The companies noted that Clause 7.2 stated, 'Material must be sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine'. Boehringer Ingelheim and Lilly alleged a breach of Clause 7.2.

In addition, whilst there were several Januvia claims on page 4 of the leavepiece, no Januvia data was presented in the leavepiece to support the claims made.

Boehringer Ingelheim and Lilly alleged that as the exaggerated bar chart was followed immediately by claims of Januvia's efficacy and safety readers would draw indirect comparisons between Januvia and linagliptin.

Boehringer Ingelheim and Lilly submitted that in their view the leavepiece disparaged linagliptin and misled readers and alleged a failure to uphold high standards in breach of Clause 9.1.

RESPONSE

Merck Sharp & Dohme denied that the leavepiece was in breach of Clauses 7.2, 7.3 and 9.1.

Merck Sharp & Dohme submitted that Gallwitz *et al* was the only in-licence study to compare the efficacy of linagliptin with that of an active comparator (a sulphonylurea, the default second-line medicine class after metformin for type 2 diabetes according to current guidelines from the National Institute for health and Clinical Excellence (NICE)). Despite this, and the fact that the data were included in the linagliptin summary of product characteristics (SPC), and that such active comparator trials represented 'gold-standard' evidence for health professionals seeking to make rational prescribing decisions, Boehringer Ingelheim and Lilly had consistently not referred to this study in any of their own promotional materials; they preferred to rely instead on less informative placebo-controlled trials.

Merck Sharp & Dohme stated that the reason for this was self-evident: although the trial nominally demonstrated non-inferiority of linagliptin vs glimepiride, based on a broad non-inferiority criterion of 0.35% relative reduction in HbA_{1c}, the efficacy results obtained with linagliptin were less than impressive. At 52 weeks, the differential HbA_{1c} reduction between the two agents was 0.22% in favour of glimepiride (-0.6% vs -0.38%) and 0.2% at 104 weeks (-0.16% vs -0.36%). Merck Sharp & Dohme believed that most diabetologists would consider these differences to be clinically significant, and the reduction with linagliptin at 104 weeks to be virtually negligible. These results contrasted sharply with those obtained with other DPP-4 inhibitors, particularly (in this context) the trial conducted by Seck *et al* (2010), which demonstrated identical HbA_{1c} reductions of 0.5% between sitagliptin and a sulphonylurea over 2 years.

Merck Sharp & Dohme submitted that Boehringer Ingelheim and Lilly were aware of the significant question marks around the comparative efficacy of linagliptin. The European Public Assessment Report

(EPAR) for linagliptin stated, in relation to Gallwitz *et al* that:

> 'The claim of non-inferior efficacy of linagliptin compared to glimepiride (study 1218.20) [Gallwitz *et al*] is not appropriately supported by data. The pre-defined non-inferiority margin was too wide considering the treatment effects observed for linagliptin as well as glimepiride. In addition, approximately 50% of the patients did not receive the maximum dose of 4mg of glimepiride. Moreover, despite relatively low baseline HbA_{1c} values, more patients in the linagliptin group than in the glimepiride group needed rescue medication (24.7% linagliptin; 21.5% glimepiride) or discontinued the trial due to lack of efficacy (5.8% linagliptin; 1.9% glimepiride). Interestingly, data from the second part of study 1218.50 [a different trial, which investigated the efficacy of linagliptin compared with placebo and glimepiride in patients intolerant to metformin therapy] showed that the treatment with glimepiride induced a mean decrease in HbA_{1c} of 0.82%, whereas linagliptin was associated with a decrease of 0.44%, further supporting the impression that efficacy of the two agents is not similar.'

Furthermore, in Cases AUTH/2440/10/11 and AUTH/2441/10/11 (GP v Boehringer Ingelheim and Lilly) the Panel examined comparative efficacy claims for linagliptin, and concluded:

> 'The Panel considered that the claim at issue implied that Trajenta [linagliptin] offered class-comparable efficacy in all settings, i.e. whether it was used as monotherapy or in combination with other oral hypoglycaemic agents. This did not appear to be so; in all cases where figures were available, the HbA_{1c} lowering effect of Trajenta was less than with other DPP-4 inhibitors … Given the data upon which it was based, the Panel considered that the claim that Trajenta offered 'class-comparable efficacy' was misleading and could not be substantiated. A breach of the Code was ruled. The Panel considered that the statement exaggerated the properties of Trajenta, and a further breach of the Code was ruled.'

Also of interest from the Panel's ruling in the same case was the statement 'The Panel noted that the claim [of class-comparable efficacy] was based on an indirect comparison of efficacy data from various sources'. It would seem that Boehringer Ingelheim and Lilly were content to use indirect comparisons in an attempt to substantiate a blanket efficacy claim (ruled by the Panel to be inadmissible), but were notably more purist about the use of indirect comparisons that were not to linagliptin's advantage. In the absence of head-to-head data, it was not unreasonable to compare the relative efficacy of two products based on their performance in very similar trials, especially where (as noted for linagliptin in the EPAR quotation, above) the efficacy results were similar across different studies.

Merck Sharp & Dohme referred to the protracted inter-company dialogue about the leavepiece which led it to believe that it could not have made any change to the bar chart which would have satisfied Boehringer Ingelheim and Lilly, short of removing it. Therefore, it appeared that the inter-company dialogue process was futile from its inception and the true purpose of the companies was to suppress any dissemination of the data from this pivotal trial. Merck Sharp & Dohme believed that prescribers should be able to draw their own conclusions as to the value and significance of Gallwitz *et al*.

Merck Sharp & Dohme submitted that it had never denied that the leavepiece was developed as a linagliptin rebuttal/objection-handler. As such, the comparative efficacy of linagliptin was a valid subject for discussion, and Merck Sharp & Dohme did not understand Boehringer Ingelheim and Lilly's assertion that a pivotal linagliptin efficacy trial, the only available study in which an active comparator was employed, would not be relevant.

Merck Sharp & Dohme saw no need to include every detail of Gallwitz *et al* in the leavepiece, including the safety and tolerability profile of linagliptin. It was well accepted that DPP-4 inhibitors exhibited low risks of hypoglycaemia and weight gain. The leavepiece was not intended as a comparison between linagliptin and sulphonylurea, but rather linagliptin and sitagliptin. It was ironic that Boehringer Ingelheim and Lilly should quote the provisions of Clause 7.2 on this point, as Merck Sharp & Dohme believed that the omission of Gallwitz *et al* from their own materials rendered them insufficiently complete to enable recipients to form their own opinion of the therapeutic value of linagliptin.

Merck Sharp & Dohme submitted that all the Januvia claims in the leavepiece were referenced and substantiable. As such, there was no requirement under the Code to include detailed Januvia data, particularly in a piece developed for a very specific purpose and not intended as a general Januvia detail aid.

The issue of indirect comparisons was referred to above. In the absence of head-to-head studies of efficacy and safety between any two medicines in the same class, prescriber choice would inevitably depend on some form of indirect comparison. The point at issue in this case was whether prescribers should be enabled to have access to all relevant data in order to inform their treatment decisions as fully as possible.

Merck Sharp & Dohme submitted that it had been fair in representing the Gallwitz *et al* data and ensured that recipients of the leavepiece were provided with the necessary information to make an informed decision. The fact that Boehringer Ingelheim and Lilly considered a fair representation of data with their own product to be 'disparaging' was telling in itself.

In conclusion, the use of rebuttal/objection-handlers was well-established in the pharmaceutical industry. The representatives' briefing material for the original version of the leavepiece made it clear that the leavepiece was not intended for general

use, but only for well-defined linagliptin 'hotspot' areas, ie areas in which linagliptin represented a significant commercial challenge. As such, data on the comparative efficacy of linagliptin was highly relevant. Furthermore, the leavepiece had not been made generally available to representatives – a specific written request had to be made to the brand management team, outlining the reasons for use.

Merck Sharp & Dohme submitted that it had not 'cherry-picked' Gallwitz *et al* – it was the only trial in which linagliptin was compared with an active comparator (indeed the active comparator given that sulphonylureas were the default second-line medication class according to NICE guidelines). As such, Gallwitz *et al* was the most informative available study on the comparative efficacy of linagliptin. The current version of the leavepiece was fair in representing these efficacy data. Although Merck Sharp & Dohme agreed with the EPAR assessment that the pre-specified, non-inferiority criterion in Gallwitz *et al* was drawn so broadly as to be practically meaningless, it had nevertheless noted in bold typeface that linagliptin was non-inferior above the bar chart at issue, and the non-inferiority margin was also specified below the chart. In addition, the briefing material made it quite clear that, when discussing the study, if doubts were raised about the efficacy of linagliptin, the representative was obliged to state the non-inferiority finding.

Merck Sharp & Dohme believed that it had acted in good faith throughout the inter-company dialogue process, and had made every effort to accommodate Boehringer Ingelheim and Lilly's concerns. It regretted that this matter had been referred to the PMCPA, but it appeared that nothing it could have done would have satisfied Boehringer Ingelheim and Lilly other than removal of any reference to Gallwitz *et al*.

PANEL RULING

The Panel noted that the leavepiece at issue (ref DIAB-1061227) had been superseded in January 2013 by closely similar material (ref DIAB-1067466) which addressed some of the concerns raised in inter-company dialogue.

The Panel noted Boehringer Ingelheim and Lilly's remaining concern that the leavepiece would raise doubts in the reader's mind about the efficacy of linagliptin. The companies had further noted that the Code stated that 'material must be sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine'. The Panel noted that although that quotation from the Code appeared to relate to what a company stated about its own medicine, the same was true for what a company stated about its competitor.

The Panel noted that the leavepiece was to be used in well-defined linagliptin 'hot spots' ie in areas where linagliptin represented a significant commercial challenge. As such, Merck Sharp & Dohme had submitted that data on the comparative efficacy of linagliptin was highly relevant. The representatives' briefing material stated that the leavepiece was to be used proactively to distinguish Januvia and Janumet (sitagliptin/metformin combination) from linagliptin. Merck Sharp & Dohme had also stated that the leavepiece was not intended as a comparison between linagliptin and sulphonylurea, but rather linagliptin and sitagliptin. Given the purpose of the leavepiece, the Panel did not consider that the omission of the hypoglycaemia and body weight results from Gallwitz *et al* which compared linagliptin and glimepiride was unacceptable. No breach of Clause 7.8 was ruled.

The Panel noted that the only efficacy data presented regarding linagliptin was the bar chart depicting the results of Gallwitz *et al* which showed that at one year linagliptin lowered HbA_{1c} by 0.38% and at two years by 0.16%. The Panel noted that the two year figure was within the non-inferiority margin of 0.35%. The Panel noted the purpose of the leavepiece ie to compare the efficacy of linagliptin with that of sitagliptin and it queried whether Gallwitz *et al*, in isolation, gave an accurate and balanced overview of the efficacy of linagliptin. Studies (other than Gallwitz *et al*) cited in Section 5.1 of the Trajenta (linagliptin) SPC referred to reductions in HbA_{1c} compared to placebo ranging from -0.72% after 52 weeks (in patients with severe renal impairment with linagliptin as monotherapy) to -0.57% at 18 weeks (linagliptin as monotherapy). In that regard the Panel queried whether the results of Gallwitz *et al* were outliers ie a reduction of 0.16% at 2 years. The Panel acknowledged that the results from all of the trials cited in the Trajenta SPC could not be directly compared but nonetheless such data suggested that the reduction in HbA_{1c} that could be expected from the medicine might be more in the region of -0.5-0.6% as opposed to the -0.38% and -0.16% reported by Gallwitz *et al*. The Panel did not consider that the use of Gallwitz *et al*, in isolation, provided a fair and balanced overview of the efficacy of linagliptin. In the Panel's view, readers would see the figures of -0.38% and -0.16% and assume that was the standard HbA_{1c} lowering effect of linagliptin which was not so. Merck Sharp & Dohme had stated that it believed that most diabetologists would consider the HbA_{1c} reduction with linagliptin at 104 weeks to be virtually negligible. The Panel considered that the bar chart would unfairly raise doubts about the clinical value and efficacy of linagliptin as alleged and was misleading in that regard. A breach of Clause 7.2 was ruled. The Panel did not consider that the bar chart gave a clear, fair and balanced view of the efficacy of linagliptin. A breach of Clause 7.8 was ruled.

The Panel noted that the page of the leavepiece which featured the bar chart was followed by a page listing the key selling points of Januvia. The Panel noted the complainants' concern that no data was presented in the leavepiece to support the claims made. In that regard the Panel noted that substantiating data did not have to be presented in promotional material but that all claims had to be capable of substantiation. There was no allegation that the claims could not be substantiated and the Panel further noted that all of the claims were referenced and a list of references was included.

One of the key selling points listed was 'Significant HbA_{1c} reductions'. In the Panel's view, given the stated purpose of the leavepiece, the reader would draw an indirect comparison between this claim and the very small reductions in HbA_{1c} depicted for linagliptin in the bar chart on the previous page. The Panel noted its comments above about the data depicted in the bar chart and considered that the comparison between linagliptin and Januvia was thus misleading. A breach of Clause 7.3 was ruled.

The Panel noted its rulings above and considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

Complaint received **28 February 2013**

Case completed **15 April 2013**

CASE AUTH2583/3/13

ALMIRALL v LEO

Picato advertisement

Almirall complained about a journal advertisement for Picato (ingenol mebutate) gel issued by Leo Pharma. The advertisement employed the image of a high speed train which Almirall submitted reinforced the claims 'Announcing the arrival of... The revolutionary, shortest duration, patient-applied actinic keratosis treatment'. Almirall alleged that the advertisement was misleading and that the claims and the visual imagery were exaggerated and all embracing.

Almirall noted that Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults ie actinic keratosis grade 1. The advertisement implied that Picato was licensed for any type of actinic keratosis and failed to clarify its more restricted indication.

Almirall alleged that the decription of Picato as being 'shortest duration, patient-applied treatment' was misleading because it appeared to suggest that the clinically relevant, therapeutic *effect* of treatment (ie complete healing of actinic keratoses), was the most rapid available, which was not so. Whilst the application was over 2 or 3 days, the summary of product characteristics (SPC) stated that optimal therapeutic effect should be assessed after 8 weeks when, if the treatment area showed an incomplete response, the treatment should be carefully re-evaluated and management reconsidered.

The SPC stated that Picato had to be stored between 2 and 8ºC; however this was not reflected in the prescribing information. Almirall alleged that this was misleading.

Almirall alleged that high standards had not been maintained.

The detailed response from Leo is given below.

The Panel noted that the advertisement was headed 'Picato Announcing the arrival of...The revolutionary, shortest duration, patient-applied actinic keratosis treatment'. Below the claim were two spiral bound pads one showing '2 DAYS' and the other showing '3 DAYS'. To the left of the pads was the depiction of a high speed train which appeared to be on the move.

The Panel noted that Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults. The headline claim, however, only referred to actinic keratosis without noting the licence restriction. It appeared that Picato could treat any type of actinic keratosis which was not so. The Panel did not consider that the advertisement encouraged rational use and a breach was ruled.

The Panel noted that patients had to apply Picato gel to the affected area once daily for two or three consecutive days depending on the site affected. The Panel noted Leo's submission that this was 'revolutionary' in that other treatment options had to be applied for 21-90 days. The Panel accepted that for patients, only having to apply treatment once daily for two or three consecutive days as opposed to 21-90 days would be seen as a radical change. The Panel considered, however, that from the claim, 'The revolutionary, shortest duration, patient-applied actinic keratosis treatment', it was not entirely clear that 'revolutionary' referred only to 'shortest duration' and not also to the 'patient-applied actinic keratosis treatment'. The claim together with the image of the high speed train might be taken to relate to the speed of effect of Picato. In that regard the Panel noted that the optimum effect of treatment could only be assessed approximately 8 weeks (56 days) after treatment. The Panel considered that the claim was exaggerated as alleged. A breach of the Code was ruled.

The Panel considered that although Picato had to be stored in a refrigerator (2ºC-8ºC) omission of this information from the prescribing information did not mean that there had been a failure to provide the information required and no breach of the Code was ruled.

The Panel noted its rulings above and in particular its ruling that the advertisement did not encourage the rational use of the medicine. The Panel considered that high standards had not been maintained. A breach of the Code was ruled.

Almirall Ltd complained about an advertisement (ref 4340a/00016(1)) for Picato (ingenol mebutate) gel issued by Leo Pharma and published in the BMJ 26 January 2013. Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults.

COMPLAINT

Almirall noted that the advertisement employed the image of a high speed train to reinforce the claims 'Announcing the arrival of... The revolutionary, shortest duration, patient-applied actinic keratosis treatment'. Almirall alleged that the advertisement was misleading and that the claims and the visual imagery were exaggerated, all embracing and clearly in breach of Clauses 7.10 and 9.1. Almirall also alleged a breach of Clause 4.2.

Almirall noted the requirements of Clause 7.10 and its supplementary information which warned against the use of superlatives, all embracing terms (such as 'the', 'revolutionary' etc) unless they could be clearly substantiated.

Almirall noted that Section 4.1 of the Picato summary of product characteristics (SPC) clearly stated that Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults ie actinic keratosis grade 1. The Picato advertisement implied that Picato was licensed for any type of actinic keratosis and failed to give adequate information, consistent with the SPC, to clarify its more restricted indication.

Picato was described as being 'shortest duration, patient-applied treatment'. Even though the technical dictionary definition of 'treatment' might relate to its time of physical application, Almirall alleged that the claim was misleading because it appeared to suggest that the clinically relevant, therapeutic *effect* of treatment (ie complete healing of actinic keratoses), was the most rapid available, which was not so. Almirall submitted that inadequate care had been taken to avoid misleading the prescriber on this point; whilst the application was indeed over 2 or 3 days, Section 4.2 of the SPC stated that optimal therapeutic effect should be assessed 8 weeks after treatment, adding that if the treatment area showed an incomplete response at the follow-up examination, the treatment should be carefully re-evaluated and management reconsidered.

Almirall noted that Clause 4.2 required prescribing information to contain a succinct statement of the information in the SPC which related to the dosage and method of use relevant to the indications quoted in the advertisement. The SPC stated that Picato had to be stored between 2 and 8 degrees Celsius; however this was not reflected in the prescribing information. Almirall alleged that this was misleading and had the potential to lead to improper storage and usage of Picato which could compromise both its claimed efficacy and safety.

In view of the shortcomings described above, Almirall alleged that there had been a serious failure to maintain high standards in the creation and review of this advertisement against Code requirements, with scant regard shown to the special nature of the audience to which the advertisement was targeted.

RESPONSE

Leo stated that Picato was indicated for all actinic keratosis, with the exception of hyperkeratotic and hypertrophic actinic keratosis, in adults and this was clearly stated in the prescribing information on the advertisement; thus it did not consider that this part of the advertisement was misleading. In addition, the prescribing information was clearly displayed as part of the advertisement. Leo therefore disputed the allegation that the advertisement implied that Picato was licensed for any type of actinic keratosis and failed to give adequate information, consistent with the SPC, to clarify its more restricted indication.

With regard to the claim 'shortest duration, patient-applied treatment', Leo submitted that the technical definition of treatment related to the time of its physical application, ie the number of days of administration (2 or 3 days). Therefore, Picato was the shortest duration, patient-applied treatment for actinic keratosis.

With regard to the word 'revolutionary' and the context in which it was used, Leo noted that the Oxford English Dictionary defined the word as 'involving or causing a complete or dramatic change'. Leo stood by this claim, as it believed this patient-applied topical treatment, with a duration of just 2 or 3 days (depending on the site of treatment), was considerably shorter than the current treatment duration of 21-90 days. Hence, the word 'revolutionary' was substantiated. Leo submitted that during pre-vetting, the Medicines and Healthcare Products Regulatory Agency (MHRA) had asked the company to make it clear that 'revolutionary' related to the short treatment duration. Leo submitted that this was clear from the advertisement.

Leo did not consider that there was a point to answer in relation to Clause 4.2 as the prescribing information did not usually contain information on the pharmaceutical precautions, but focused on the clinical information. Leo submitted that this was in line with PMCPA guidance. The Picato prescribing information included information about the dosage and method of use consistent with Section 4.2, Posology and Method of Administration, of the SPC, as per the Code requirements.

The SPC, referred to in the prescribing information, included information on storage and the instruction 'Store in a refrigerator' was clearly indicated on the front of the product carton.

In view of the above, Leo did not consider that it had breached the Code and it had therefore maintained high standards.

PANEL RULING

The Panel noted that the advertisement was headed 'Picato Announcing the arrival of...The revolutionary, shortest duration, patient-applied actinic keratosis treatment'. Below the claim were two spiral bound pads one showing '2 DAYS' and the other showing '3 DAYS'. To the left of the pads was the depiction of a high speed train which appeared to be on the move.

The Panel noted that Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults. The headline claim, however, only referred to actinic keratosis without noting the licence restriction. It appeared that Picato could treat any type of actinic keratosis which was not so. In that regard the Panel did not consider that the advertisement encouraged the rational use of the medicine. The provision of the indication in full in the prescribing information did not negate the otherwise misleading impression. A breach of Clause 7.10 was ruled.

The Panel noted that for the treatment of actinic keratosis on the trunk or extremities, patients had to apply one tube (0.47g) of Picato 500mcg/g to the affected area once daily for two consecutive days. If the patient had actinic keratosis on the face and scalp then one tube (0.47g) of Picato 150mcg/g had to be applied to the affected area once daily for three consecutive days. The Panel noted Leo's submission that Picato treatment was 'revolutionary' in that other treatment options had to be applied for 21-90

days. The Panel noted that the dictionary defined something as being 'revolutionary' if it involved or constituted radical change. The Panel accepted that for patients, only having to apply treatment once daily for two or three consecutive days as opposed to 21-90 days would be seen as a radical change. The Panel considered, however, that from the claim, 'The revolutionary, shortest duration, patient-applied actinic keratosis treatment', it was not entirely clear that 'revolutionary' referred only to 'shortest duration' and not also to the 'patient-applied actinic keratosis treatment'. The claim together with the image of the high speed train might be taken to relate to the speed of effect of Picato. In that regard the Panel noted that the optimum effect of treatment could only be assessed approximately 8 weeks (56 days) after treatment. The Panel considered that the claim was exaggerated as alleged. A breach of Clause 7.10 was ruled.

The Panel noted that tubes of Picato had to be stored in a refrigerator (2°C-8°C). This was not stated in the prescribing information included in the advertisement. The Panel noted that Clause 4.2 listed the components of prescribing information; storage conditions of the medicine were not included. The Panel thus did not consider that in omitting the storage requirements for Picato from the prescribing information there had been a failure to provide the information listed in Clause 4.2. Clause 4.1 required the prescribing information listed in Clause 4.2 to be provided and so the Panel ruled no breach of Clause 4.1.

The Panel noted its rulings above and in particular its ruling that the advertisement did not encourage the rational use of the medicine. The Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

Complaint received **4 March 2013**

Case completed **4 April 2013**

PHARMACIST v ALMIRALL

Invitation to a meeting

A clinical pharmacist complained about a meeting invitation from Almirall.

The first page of the four page invitation was headed 'Eklira Genuair' followed by the non-proprietary name (aclidinium bromide inhalation powder). Beneath that was stated 'COPD [chronic obstructive pulmonary disease] Management Guidelines'. Page 2 gave a brief overview of the meeting, one of the speakers and the company. The prescribing information was on the final page.

The complainant noted that the invitation prominently displayed the name of the medicine and the prescribing information yet the meeting appeared to be educational and covered COPD management guidelines. The complainant understood that promotional and educational activities must be separate and alleged that placing the name of the medicine on the invitation to an educational meeting clouded this boundary. The complainant also noted that educational goods and services must not bear the name of a medicine and wondered whether this would include the invitation.

The detailed response from Almirall is given below.

The Panel considered that it was clear that the invitation and meeting were promotional. The product name and company logo featured prominently on the front page of the invitation. The meeting was initiated and funded by Almirall and the invitation was signed by a medical representative.

The Panel noted that the meeting would, *inter alia,* look at existing guidelines for the management of COPD. The presentations included a discussion of the relevant guidelines, diagnosis and assessment of COPD and various inhaled therapy treatment options. A section entitled 'The emerging COPD environment' featured slides on Almirall's product. Oral therapies were also reviewed. The management of exacerbations and early intervention and commissioning to improve outcomes in COPD were also discussed. The Panel noted that whilst delegates would find certain aspects of the meeting informative and helpful it nonetheless satisfied the broad definition of promotion.

The Panel did not consider that the promotional nature of the invitation had been disguised. Its promotional nature was clear from the outset. No breach of the Code was ruled.

The Panel noted that medical and educational goods and services were non promotional material and activities which enhanced patient care and benefited the NHS. These requirements did not apply to promotional material such as the invitation in question. No breach of the Code was ruled.

A clinical pharmacist complained about a meeting invitation from Almirall which he had received via a colleague.

The first page of the four page invitation was headed 'Eklira Genuair' followed by the non-proprietary name (aclidinium bromide inhalation powder). Beneath that was stated 'COPD [chronic obstructive pulmonary disease] Management Guidelines'. Page 2 gave a very brief overview of the meeting, one of the speakers and the company and page 3 detailed the agenda, date, time and venue. The prescribing information for Eklira Genuair was on page 4.

Eklira Genuair was indicated as maintenance broncodilator treatment to relieve symptoms in adult patients with COPD.

COMPLAINT

The complainant noted that the invitation prominently displayed the name of the medicine and the prescribing information yet the meeting appeared to be educational and covered COPD management guidelines.

The complainant stated that he understood that promotional and educational activities must be separate and that placing the name of the medicine on the invitation to an educational meeting clouded this boundary.

The complainant was advised that his complaint was being considered in relation to Clause 12.1. In response the complainant agreed that Clause 12 was worthy of scrutiny but in addition referred to Clause 18.4 that educational goods and services must not bear the name of a medicine and wondered whether this would include the invitation.

When writing to Almirall, the Authority requested that it consider the requirements of Clauses 12.1 and 18.4.

RESPONSE

Almirall submitted that it had recently launched a new respiratory product, Eklira Genuair. On the invitations for regional launch meetings, in order to ensure that attendees were clear that they were company-sponsored meetings, Almirall had included the product name and prescribing information as well as a sponsorship statement. Almirall considered that this left no ambiguity for the recipient that this was a company-sponsored meeting that had been organised by the sales team and would include discussion of the product it was promoting.

When the invitation was sent out, although the topics for the meeting were confirmed, the slides from the presenters with the exact content were not available for review. Almirall stated that in view of this, it was careful to specify in the invitation that new treatment options would be discussed. Almirall stated that it included the product branding to avoid any doubt that this would include its own newly launched product which belonged to a class recommended in COPD guidelines. Almirall thus disagreed that the meeting invitation or agenda could be seen as disguised promotion, and considered that if anything it had erred on the side of caution by making it explicitly clear that the meeting would be promotional by prominently including the product name and prescribing information.

Almirall noted that the supplementary information to Clause 19.1 stated that all meetings must have a clear educational content, which it had ensured applied to these meetings. Almirall did not know of any requirements in the Code which stated that educational material could not be promotional, or vice versa.

Almirall queried whether the complainant might have thought that the requirement of Clause 18.4 that medical and educational goods and services must not bear the name of any medicine, applied to company-sponsored meetings which also had an educational content. However, Almirall stated that this meeting was not a medical and educational service, it was a company-sponsored, promotional, launch meeting, and so was subject to the requirements of Clause 19.

PANEL RULING

The Panel noted that Clause 1.2 of the Code defined promotion as any activity undertaken by a pharmaceutical company or with its authority which promoted the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines. The Panel further noted the supplementary information to Clause 19.1 Meetings and Hospitality stated that with any meeting there must be a clear educational purpose. The supplementary information also listed examples of meetings which pharmaceutical companies could appropriately hold or sponsor including launch meetings for new products. Launch meetings would be promotional and therefore trigger certain requirements in the Code including the requirement to include prescribing information.

The Panel considered that it was clear that the invitation and meeting were promotional. The product name and company logo featured prominently on the front page of the invitation. The brief synopsis of the meeting made it clear that it would look at new treatment options. The meeting was described as initiated and funded by Almirall and the invitation was signed by a medical representative. Prescribing information appeared on the back outside cover.

The Panel noted that the meeting would, *inter alia*, look at existing guidelines for the management of COPD. The presentations included a detailed discussion of the relevant guidelines, diagnosis and assessment of COPD followed by an in depth discussion of various inhaled therapy treatment options. A section entitled 'The emerging COPD environment' featured 32 slides on Almirall's product and inhaler Eklira Genuair and 10 slides on a long-acting muscarinic antagonist. Oral therapies were also reviewed. Other matters such as management of exacerbations and early intervention and commissioning to improve outcomes in COPD were also discussed. The Panel noted that whilst delegates would find certain aspects of the meeting informative and helpful it nonetheless satisfied the broad definition of promotion set out in Clause 1.2.

The Panel did not consider that the promotional nature of the invitation had been disguised. Its promotional nature was clear from the outset. No breach of Clause 12.1 was ruled.

The Panel noted that medical and educational goods and services described in Clause 18.4 were non promotional material and activities which enhanced patient care and benefited the NHS. The requirements of Clause 18.4 did not apply to promotional material such as the invitation in question. No breach of Clause 18.4 was ruled.

Complaint received **7 March 2013**

Case completed **16 April 2013**

CASE AUTH/2586/3/13

VOLUNTARY ADMISSION BY FERRING

Symposium flyers

Ferring Pharmaceuticals voluntarily admitted that two flyers for symposia to be held at a European congress in Milan had been sent to UK delegates by its global colleagues by mistake.

As the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Ferring. Ferring explained that some of the sessions in the symposia were outside the current UK licences for its products and so the flyers were not intended to be sent to UK delegates. It was attempting to stop and recall the mailings where it could.

The response from Ferring is given below.

The Panel noted that the company's corporate office in Geneva had sent invitations to two company sponsored symposia to, *inter alia*, 436 UK registered delegates. Data presented at the symposia about Ferring's products included material about indications and doses not licensed in the UK. The Panel noted that under the Code Ferring UK was responsible for activity in the UK of its global colleagues where such activity was within the scope of the Code.

The Panel considered that the distribution of invitations to UK delegates for an overseas meeting came within the scope of the Code. In addition, the Panel noted that the Code required all meetings which involved travel outside the UK to be certified in advance.

The Panel noted that one of the invitations was headed 'Ferring invites you to a satellite symposium: New data on androgen deprivation with a GnRH [gonadotrophin releasing hormone] antagonist: improving patient outcomes in prostate cancer'. Reference was made to an increasing volume of comparative data now available for the GnRH antagonist degarelix (Ferring's product, Firmagon) and LHRH (leuteinizing hormone-releasing hormone) agonists. The Panel noted that the invitation mentioned the product and therapy area and thus the Panel considered that it was promotional material. It had not been certified as required by the Code and a breach was ruled.

The second invitation was to a symposium entitled 'Nocturia: definitive diagnosis for better patient outcomes' which included presentations on 'Breaking the Patient stereotype'; 'What is different about Nocturia?', 'Non-antidiuretic vs antidiuretic pharmacology for nocturia'; followed by a round up of patient case studies. The invitation explained that research supported the treatment as a distinct disorder and explained that it was not necessarily driven by lower urinary tract symptoms but that it could result from multiple underlying causes. A strapline at the bottom of the invitation stated 'Ferring does not have a product licensed for Nocturia in Italy'.

The Panel noted that in the UK Ferring's product Desmospray (desmopresin) was indicated for, *inter alia*, the treatment of nocturia associated with multiple sclerosis where other treatments had failed. Desmomelt and Desmotabs (both desmopressin) were each indicated for the treatment of primary nocturnal enuresis. The Panel noted that whilst the invitation did not directly mention Ferring's products it did discuss nocturia and that the condition could be caused by conditions other than those involving the bladder, prostate, or urethra. The Panel considered that the invitation went beyond a general discussion of nocturia and was closely linked to the licensed indication for Desmospray. The invitation was promotional in this regard. It had not been certified as required by the Code and a breach was ruled.

The Panel noted that according to Ferring each symposium included data that was outside each product's UK licence. This was not clear from either invitation which included only a general description of the products' licensed indications. The Panel noted that Ferring's admission related solely to the invitations and on that basis the Panel ruled no breach of the Code as neither invitation promoted the products in a manner that was inconsistent with their marketing authorizations.

Ferring Pharmaceuticals Ltd voluntarily admitted that two flyers for symposia to be held at a European congress in Milan had been sent to UK delegates by its global corporate office by mistake.

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

COMPLAINT

Ferring advised the Authority that a letter with two invitation flyers for Ferring-sponsored symposia, to be held at the European Association of Urology (EAU) Annual Congress in Milan on 17/18 March 2013, was sent in error to all UK delegates registered to attend the congress. The flyers were sent by global colleagues on 5 March 2013 without UK approval. The two symposia were: Nocturia: Definitive diagnosis for better patient outcomes and new data on androgen deprivation with a [gonadotrophin releasing-hormone] GnRH antagonist: Improving patient outcomes in prostate cancer.

Ferring explained that some of the sessions in the symposia were outside the current UK licences for its products and so the flyers were not intended to be

sent to UK delegates. The company was attempting to stop and recall the mailings where it could. The matter had been discussed with global colleagues and robust measures were now in place to improve internal communication and prevent such incidents from happening again.

When writing to Ferring, the Authority asked it to respond to Clauses 3.2 and 14.1 of the Code.

RESPONSE

Ferring submitted that the annual EAU Congress was one of the world's leading, independent, research based urology conferences. In conjunction with this congress, Ferring sponsored two scientific symposia that were organised and conducted by a number of experts from the relevant therapeutic fields. These symposia were:

'Nocturia: Definitive diagnosis for better patient outcomes' which aimed to provide an overview of the variety of clinical characteristics of patients with nocturia, and the multifactorial nature of the mechanism of the disease. The symposium included presentations that reviewed the prevalence and consequences of nocturia, discussed case studies of patients with nocturia and their diagnoses, reviewed current understanding of the mechanism of nocturia and discussed treatment algorithms and guidelines, and finally summarised the evidence for efficacy of available pharmacotherapies for nocturia.

'New data on androgen deprivation with a GnRH antagonist: Improving patient outcomes in prostate cancer' which aimed to present recent data on androgen deprivation therapy for prostate cancer, in a clinically meaningful way that facilitated improved patient care.

Ferring submitted that the two symposia provided scientific information about actual trial data and analyses. While in many countries Ferring marketed desmopressin for the treatment of nocturia and a GnRH antagonist, degarelix (Firmagon), for the treatment of prostate cancer, the symposia did not promote these medicines. Rather they were traditional scientific symposia under the control of independent scientific experts. Information presented at the symposia included clinical data about desmopressin and degarelix, including data about indications and dose regimes not licensed in the UK.

Sponsored satellite symposia were organised within the official EAU Congress scientific programme and the speakers' honoraria directly paid by EAU. The scientific outline was endorsed by the chairman and communicated to health professionals attending the congress. Flyers were usually printed to inform the delegates about the topic and, in this case, had been handed out by many companies sponsoring similar symposia at this meeting. The flyers reflected the content of the symposia described above, which provided information about the state of the art for nocturia and prostate cancer disease management and treatments. Neither the symposia, nor the flyers were promotional.

Ferring stated that the flyers were approved by the company's corporate office and its Italian affiliate and complied with the relevant Italian regulations. The timelines for approval by the Italian regulatory authority were given.

Ferring noted that the relevant standard operating procedure (SOP) (CS-10237, Approval of therapy area and product specific promotional and non-promotional marketing material) stated on page 5 that 'When Global Marketing Material is produced for a congress, the [regulatory affairs manager] and/or General Manager of the country where the congress will be held must review the material and ensure that it complies with the local regulation'. This SOP had been strictly followed in the preparations for the symposia.

The Ferring corporate office decided to send the flyers to the list of EAU pre-registered delegates provided by EAU. Unfortunately, all 436 UK registered delegates were mistakenly included in the bulk mailing sent by the mailing company, although this activity had not been notified to, or approved by Ferring UK. The flyers were sent to all registered delegates, approximately two weeks before the congress.

Ferring noted that Clause 3.2 stated that the promotion of a medicine must be in accordance with the terms of its marketing authorization and must not be inconsistent with the particulars listed in its summary of product characteristics. Ferring further noted that the flyers did not mention the name of any particular medicine and the symposia at issue were balanced programmes for the purpose of legitimate scientific exchange.

Ferring noted that Clause 14.1 stated that promotional material must not be issued unless its final form, to which no subsequent amendments would be made, had been certified by two persons on behalf of the company. In this case Ferring was uncertain whether the flyers were promotional items as they did not include the name of any specific product. However, Ferring UK would normally certify such items to ensure compliance with the Code, and it was because they were distributed without such review or certification that it had made the voluntary admission.

PANEL RULING

The Panel noted that the company's corporate office in Geneva had produced invitations to two company sponsored symposia and distributed them to, *inter alia*, 436 UK registered delegates. Data presented at the symposia about Ferring's products included material about indications and doses not licensed in the UK. The Panel noted that it was an established principle under the Code that the UK company was responsible for acts and omissions of its overseas affiliates that came within the scope of the Code. Ferring UK was thus responsible under the Code for the activity of its global corporate office in the UK.

The Panel noted Ferring's submission that the symposia were for the purpose of legitimate

scientific exchange and were thus not promotional. In the Panel's view it did not have to consider whether the meetings fell within the supplementary information to Clause 3 Marketing Authorization which permitted the legitimate exchange of medical and scientific information during the development of a medicine provided such exchange did not constitute promotion prohibited under Clause 3 or any other clause. The voluntary admission was only in relation to the invitations and not the actual meetings. The Panel thus made no decision on the actual meetings. The Panel considered that the distribution of 436 invitations to UK delegates for an overseas meeting was an activity which came within the scope of the Code and had to comply with it irrespective of the status of the meeting in relation to the supplementary information to Clause 3. In addition the Panel noted that the Code required all meetings which involved travel outside the UK to be certified in advance. The Panel did not know whether any UK delegates had been sponsored by Ferring to attend the conference.

The Panel noted that the four page invitation to the symposium about prostate cancer was headed 'Ferring invites you to a satellite symposium: New data on androgen deprivation with a GnRH antagonist: Improving patient outcomes in prostate cancer'. The invitation included mention of an increasing volume of comparative data now available for the GnRH antagonist degarelix and LHRH agonists. Examination of the growing database also allowed a direct comparison between these products for safety endpoints. The meeting started at 17.45 with a welcome and was followed by 4 presentations; Radiotherapy and androgen deprivation,' 'Is intermittent androgen deprivation really equivalent to continuous therapy?', 'Disease control: Comparative data from degarelix vs. LHRH agonists', and 'Cardiovascular risk and ADT: New data, new insights' and finished with a panel discussion and concluding remarks. The Panel noted that Ferring's product, degarelix, was the only medicine mentioned. The front page and outside back cover featured Ferring's corporate logo within a statement 'Supported by an educational grant from Ferring Pharmaceuticals'.

The Panel noted that Firmagon (degarelix) was a gonadotrophin releasing hormone antagonist for the treatment of advanced hormone dependent prostate cancer. The Panel noted that the invitation mentioned the product and therapy area and considered that it was promotional material. It had not been certified as required by Clause 14.1 and a breach of that clause was ruled.

The Panel noted that the second invitation was for an evening symposium sponsored by Ferring entitled 'Nocturia: Definitive diagnosis for better patient outcomes' which according to its agenda covered presentations on 'Breaking the Patient stereotype'; 'What is different about Nocturia?', 'Non-antidiuretic vs antidiuretic pharmacology for nocturia'; followed by a round up of patient case studies concluding with a question and answer session. The invitation explained that research supported the treatment as a distinct disorder and explained that it was not necessarily driven by lower urinary tract symptoms but that it could result from multiple underlying causes. A strapline at the bottom of the invitation stated 'Ferring does not have a product licensed for Nocturia in Italy'.

The Panel noted that in the UK Ferring's product Desmospray (desmopressin) was indicated for, *inter alia*, the treatment of nocturia associated with multiple sclerosis where other treatments had failed. Desmomelt and Desmotabs (both desmopressin) were each indicated for the treatment of primary nocturnal enuresis. The Panel noted that whilst the invitation did not directly mention Ferring's products it did discuss nocturia and that the condition could be caused by conditions other than those involving the bladder, prostate, or urethra. The Panel considered that the invitation went beyond a general discussion of nocturia and was closely linked to the licensed indication for Desmospray. The invitation was promotional in this regard. It had not been certified as required by Clause 14.1 and a breach of that clause was ruled.

The Panel noted that according to Ferring each symposium included data that was outside each product's UK licence. This was not clear from either invitation which included only a general description of the products' licensed indications. The Panel noted that Ferring's admission related solely to the invitations and on that basis the Panel ruled no breach of Clause 3.2. Neither invitation promoted the products in a manner that was inconsistent with their marketing authorizations.

Complaint received **11 March 2013**

Case completed **25 April 2013**

ANONYMOUS GASTROENTEROLOGY CONSULTANT v ALMIRALL

Free stock allegedly offered as an inducement

An anonymous, non-contactable gastroenterology consultant complained that an Almirall representative had offered a colleague free stock of Constella (linaclotide) as a trial to support a formulary application. The complainant was very much against this type of promotion and considered that his/her department was compromised by the inducement.

The detailed response from Almirall is given below.

The Panel noted that the complainant had provided little to support his/her complaint and had not been party to the interaction in question. 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 that medical representatives had yet to be involved with the promotion of Constella. Healthcare development managers (HDMs) were involved with the product and pre-licence activities had centred around understanding local procedures for providing free stock of medicines. The HDMs were briefed not to discuss linaclotide or to actively solicit free stock. Post-licence, HDMs were similarly instructed not to actively solicit free stock supply of Constella. The Panel further noted that Almirall planned to provide limited free stock of Constella only after it was licensed and before it was launched.

The Panel considered that Almirall's role once it received a request for free stock was not entirely clear. It appeared that free stock would only be supplied once the relevant hospital trust had agreed and presumably followed its own procedures. In this regard it appeared that a formulary application would have had to be submitted before Constella could be supplied. To date, where free stock had been supplied, Constella had been granted provisional formulary approval pending local clinical evaluation. The Panel noted Almirall's submission that free stock was not offered as an incentive to complete a formulary application; the product would only be supplied after a positive formulary assessment (provisional or confirmed).

The Panel could not ask the complainant for more information and so it could not know exactly what had transpired between the Almirall employee and the complainant's colleague or when the interaction took place. Almirall had stated that any discussions about free stock had only arisen post-licence. The Panel did not consider that the complainant had shown, on the balance of probabilities, that his/her colleague had been offered a free supply of Constella as an inducement to submit a formulary application. No breach of the Code was ruled. The Panel thus did not consider that there was any evidence to show that the HDM or the company had failed to maintain high standards. No breaches of the Code were ruled.

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

An anonymous, non-contactable gastroenterology consultant in a named UK area complained that an Almirall Limited representative had offered free stock of Constella (linaclotide).

COMPLAINT

The complainant explained that one of his/her colleagues discussed Constella with an Almirall representative who stated that free stock could be offered as a trial to support a formulary application.

The complainant stated that he/she was very much against this type of promotion and considered that his/her department was compromised by the inducement. The complainant submitted that the representative had stated that this offer had been made across other UK trusts. The complainant alleged a breach of the Code.

When writing to Almirall, the Authority asked it to respond in relation to Clauses 2, 9.1, 15.2 and 18.1 of the Code.

RESPONSE

Almirall stated that in its view, there were two main possibilities: that the complainant objected to the provision of free stock of Constella because he/she considered that it was an inducement to prescribe as defined by Clause 18.1, or that the complainant objected more generally to the provision of free stock because he/she considered this induced clinicians to use new medicines and that this somehow compromised his/her department's normal medicines management processes.

Almirall also considered the possibility that there was something in the language or conduct of Almirall personnel, as reported to the complainant, that suggested that a therapeutic trial was offered on the condition that a formulary application would be made.

Almirall noted that the complainant was not the health professional that met the Almirall

representative but a third party reporting what he/she was told about the meeting. Almirall stated that it had, nonetheless, conducted careful interviews with the limited number of its employees that this meeting could have involved in order to assess the various possibilities.

Almirall explained that Constella was a first-in-class medicine for the symptomatic treatment of irritable bowel syndrome (IBS) with constipation (IBS-C) and was approved by the European Medicines Agency (EMA) in November 2012. Gastroenterologists specialising in IBS had been waiting for this medicine as it was the first one licensed for use in a sometimes difficult to treat subgroup of patients who were frequently referred from primary care. In response to requests for patient supply beginning in the pre-licence period, Almirall had established a process for provision of limited stock, free of charge between product licensing and the planned launch later in 2013.

As of 25 March 2013, no Almirall sales representative had discussed Constella as the team was yet to be deployed on this medicine. One healthcare development manager (HDM) covered the specific area in question and was responsible for ensuring that any supply of Constella requested by consultants occurred with the knowledge of the relevant pharmacy personnel and complied with local governance arrangements. Briefing slides were emailed to the HDMs in advance of a teleconference on 19 November. The presentation made clear the distinction between acceptable pre- and post-licence activity, the reactive nature of the supply process and the need to understand local pharmacy processes in order to comply with them. A copy of the presentation was provided.

A clinician who requested free stock of Constella had to submit a formulary application before supply was agreed within their hospital trust. Thus in all cases, NHS stakeholders were able to accept or reject the medicine based on their assessment of patient need, the product data and consideration of any longer term funding implications. In view of this, it was not clear in what sense the hospital department could have been compromised by supply of Constella as alleged. Furthermore, in cases to date in which free stock had been approved following formulary application, the product had been given only provisional formulary approval, pending evaluation of its real world performance by the clinician involved. Almirall anticipated that the same safeguard would be available within any trust approving the supply. Almirall considered that this significantly increased the opportunity for an accurate assessment of product risk:benefit before full formulary access was granted. Almirall did not understand how, if the shared objective was to benefit patients, working in partnership as it had done to provide free stock could be seen as unhelpful to the NHS.

Almirall submitted that the complainant might have misconstrued the provision of free stock (or the conversation details that were relayed to him/her indirectly) as being offered as an incentive to complete a formulary application. To frame the conversation in this manner would have been inconsistent with the knowledge and experience of the HDM who covered the complainant's area, ie the requesting gastroenterologist could only gain access to the medicine for his/her patients with a positive formulary assessment, hence both parties in the discussion would have known that completing an application was simply a pre-requisite of the usual trust process.

With regard to Clause 18.1, Almirall submitted that free stock of Constella did not constitute a gift and did not benefit or offer any pecuniary advantage to the gastroenterologist or other health professionals who might be involved. Any agreement to supply was in response to clinical demand and with the sole intention of providing patient benefit.

With regard to Clause 15.2, Almirall stated that it had spoken to the relevant HDM regarding his/her interactions with gastroenterologists to date. The HDM denied any portrayal of free stock as an inducement or trial to support a formulary application. To date the HDM team had engaged with a limited number of IBS experts and their respective medicines management colleagues to understand patient referral pathways and formulary application processes in different localities. Any discussions about free stock had arisen only during the post-licence phase (from 27 November 2012) and had been reactive, as per the briefing provided. In terms of representative involvement, only the relevant regional HDM and head office senior medical advisor had discussed the provision of free stock with any clinicians, acting in a strictly non-promotional capacity.

Almirall did not consider that there was any evidence to suggest that the HDM concerned had failed to maintain a high standard or had breached any aspect of the Code. The company suggested that to have separated discussion of free stock from discussion of the local formulary application process would have been incompatible with the requirements of Clause 17.8 ie that the provision of medicines and samples in hospitals must comply with individual hospital requirements.

Almirall did not consider that any evidence had been provided to suggest that high standards had not been maintained (Clause 9.1) and its investigation of the alleged interaction with a gastroenterologist supported this view.

Almirall stated that for the reasons stated above with regard to Clauses 18.1 and 9.1, it did not consider that it had brought discredit upon or reduced confidence in the pharmaceutical industry, either in the reactive provision of free stock *per se* or in the conduct of Almirall personnel involved in the local logistics of provision.

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. The complainant had not been party to the interaction between his/her colleague and the Almirall employee. 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 that medical representatives had yet to be involved with the promotion of Constella. HDMs were already involved with the product; pre-licence activities for the HDMs centred around understanding local procedures for providing free stock of medicines including identifying the key contacts in that process. The HDM briefing slides stated that the HDMs were not to discuss linaclotide and not to actively solicit free stock. The briefing slides referred to requests received by the medical team from clinicians that spontaneously requested free stock. Post-licence, HDMs were similarly instructed not to actively solicit free stock supply of Constella. The Panel further noted that Almirall planned to provide limited free stock of Constella only between product licensing (November 2012) and the product launch in 2013.

The Panel considered that in its response, Allmirall was not entirely clear about its role once it received a request for free stock. However it appeared that free stock would only be supplied once the relevant hospital trust had agreed and presumably followed its own procedures. In this regard it appeared from Almirall's submission that a formulary application would have had to be submitted before Constella could be supplied as free stock. In the two cases to date where free stock had been supplied, Constella had been granted provisional formulary approval pending its clinical evaluation by the clinicians concerned. The Panel noted Almirall's submission that the provision of free stock was not offered as an incentive to complete a formulary application; the product would only be supplied after a positive formulary assessment be that on a provisional or confirmed basis. The Panel further noted Almirall's submission that the provision of free stock significantly increased the opportunity for an accurate assessment of a product before full formulary status was granted.

The Panel noted that as the anonymous complainant was non-contactable it could not ask him/her for more information and so it was impossible to know exactly what had transpired between the Almirall employee (assumed to be the local HDM) and the complainant's colleague or if the interaction took place before or after Constella received its marketing authorization. Almirall had stated that any discussions about free stock had only arisen in the post-licence phase (from 27 November). The Panel did not consider that the complainant had shown, on the balance of probabilities, that his/her colleague had been offered a free supply of Constella as an inducement to submit a formulary application. No breach of Clause 18.1 was ruled. The Panel thus did not consider that there was any evidence to show that the HDM or the company had failed to maintain high standards. No breach of Clauses 9.1 and 15.2 were ruled.

The Panel noted its rulings above and ruled that there had thus been no breach of Clause 2.

Complaint received **13 March 2013**

Case completed **9 April 2013**

CASE AUTH/2588/3/13

THE DRUG AND THERAPEUTICS BULLETIN v NOVARTIS

Promotion of Seebri Breezhaler

The Drug and Therapeutics Bulletin complained about a booklet entitled 'Evidence Review of Seebri Breezhaler (glycopyrronium bromide)' issued for use in formulary packs by Novartis. Seebri Breezhaler was indicated for use in adults with chronic obstructive pulmonary disease (COPD).

The complainant alleged that page 6 of the Evidence Review contained an unsubstantiated argument for the treatment of COPD exacerbations. Under a sub-heading, 'The importance of reducing exacerbations', the second bullet point stated 'Mortality following hospital admission is higher in patients suffering a COPD exacerbation than those with a myocardial infarction at 12 months [Halpin 2008]. The 180 day mortality rate following a COPD exacerbation is 33% [Anzueto 2010] and therefore reductions in exacerbations can reduce mortality rates'.

The 180 day mortality rate following a COPD exacerbation was not 33%. Anzueto was a review article that highlighted the high mortality rate in patients admitted to hospital with an acute exacerbation of COPD. The paper cited Connors *et al* (1996) which compared outcomes in a particularly ill group of patients with acute hypercapnic respiratory failure. The Evidence Review did not clarify the group of patients to which this data applied. The complainant alleged that the statement was unhelpful and misleading.

A literature search showed that the conclusion 'and therefore reductions in exacerbations can reduce mortality rates' had not been proven. Mortality rates were higher in frequent exacerbators than infrequent exacerbators but the complainant was unaware of any study that had shown that reducing exacerbations with treatments lowered mortality. Data suggested that tiotropium might be more effective than long-acting beta agonists (Vogelmeier *et al* 2011)) but even a four year study in which mortality was a secondary endpoint failed to demonstrate a benefit from the use of tiotropium (Tashkin *et al* 2008).

The impact of glycopyrronium on exacerbations was a secondary endpoint in all the trials cited. Although the Evidence Review clarified primary and secondary endpoints, it presented data for the secondary endpoint first. Given the juxtaposition of the statements on mortality and exacerbations with the secondary endpoint data on exacerbations, readers might apply more weight to the information than was supported by evidence.

The detailed response from Novartis is given below.

The Panel noted that Anzueto reviewed, *inter alia*, the impact of exacerbations on mortality and noted that Connors *et al* reported that in patients admitted to hospital with acute hypercapnic respiratory failure, the 180 day mortality rate was 33%. The complainant stated that this was a particularly ill group of patients and that the 180 day mortality rate was not 33%. The complainant had not stated whether he considered the 180 day mortality rate to be more or less than 33%. The Panel noted that Seneff *et al* reported that in a group of patients aged 65 years or older admitted to intensive care primarily with an acute exacerbation of COPD, 180 day mortality was 47%. The Panel noted the difference in 180 day mortality rates between the two groups and also that there was no way of comparing the COPD severity of the two groups. Given the difference in the 180 day mortality rate reported in the literature, the Panel considered that the unqualified, unconditional claim 'The 180 day mortality rate following a COPD exacerbation is 33%' was misleading. It implied that the 180 day mortality in any patient following a COPD exacerbation had been categorically proven to be 33% which was not so. Breaches of the Code were ruled.

The Panel noted that the claim, 'and therefore reductions in exacerbations can reduce mortality rates', was not referenced. The Panel did not accept Novartis' submission that the claim was not linked to any specific treatment. Given the data on the facing page about Seebri Breezhaler and exacerbations there was an inference that Seebri Breezhaler would have a positive impact on mortality. The Panel further noted Novartis's submission that no single study had successfully demonstrated that a specific COPD treatment had decreased overall mortality. Halpin reviewed COPD treatment and noted that although the ISOLDE study showed that inhaled fluticasone significantly reduced the rate of exacerbations, a post hoc analysis only showed a non-significant trend towards improved survival (Briggs *et al* 2006). However, in the TORCH study, although fluticasone reduced the rate of exacerbation, it did not show a reduction in all-cause mortality at 3 years vs placebo (Calverley *et al* 2007). Halpin also reported that tiotropium had been shown to reduce exacerbation frequency and that a post hoc analysis suggested that it might reduce the rate of decline of FEV1; if this was a real effect then it might have an effect on mortality. Halpin further reported the benefits to COPD patients in preventing exacerbations of adding inhaled corticosteroids to long-acting B2-agonists but the studies cited did not link this benefit to a decrease in mortality. Conversely, other studies which examined the impact of adding inhaled corticosteroids to bronchodilator therapy did not link the reduced risk of death with a reduced rate of exacerbation. Halpin acknowledged that the studies reviewed, with the exception of the

TORCH study, were not designed to assess mortality rates – most were underpowered as death was an uncommon event. The Panel noted that the complainant had referred to Tashkin *et al* and Vogelmeier *et al*, neither of which had been cited by Halpin. The complainant noted that these studies showed that although tiotropium was possibly more effective than long-acting B2-agonists, in a study that compared time to first exacerbation of COPD, a four year study in which mortality was a secondary endpoint failed to demonstrate a benefit from the use of tiotropium.

Overall, the Panel considered that although the strong claim that 'reductions in exacerbations can reduce mortality rates' appeared to be self-evident, it did not reflect the balance of the data. The claim implied that reducing COPD exacerbations with treatment had been unequivocally shown to reduce mortality rates which was not so. The Panel considered that the claim was misleading as alleged and could not be substantiated. Breaches of the Code were ruled.

The Panel noted that the page facing that considered above was headed 'Glycopyrronium and exacerbations' and featured a table which detailed the secondary outcomes from the GLOW-1 study (glycopyrronium vs placebo) and the GLOW-2 study (glycopyrronium vs tiotropium). In both studies the primary efficacy endpoint was trough FEV1 at 12 weeks. Above the table was an explanation that a secondary objective of the two studies was to explore the first COPD exacerbation with glycopyrronium vs placebo over 26 weeks (GLOW-1) and 52 weeks (GLOW-2). Exploratory endpoints for GLOW-2 also included measuring the effect of glycopyrronium vs tiotropium in time to first exacerbation. The table, however, had two columns headed 'Endpoint' and 'Result' and so the secondary nature of the endpoints detailed within was not immediately obvious. The Panel considered that the explanation of the endpoints above the table was not prominent and thus was insufficient in this regard. The Panel considered that the presentation of the data was not sufficiently complete to allow the reader to appreciate its statistical significance and the table was misleading in that regard. A breach of the Code was ruled.

Given its rulings above, the Panel ruled a further breach as high standards had not been maintained.

The Drug and Therapeutics Bulletin complained about a 16 page 'Evidence Review of Seebri Breezhaler (glycopyrronium bromide)' (ref SBH12-CO17) issued for use in formulary packs by Novartis Pharmaceuticals UK Ltd. Seebri Breezhaler was indicated as maintenance bronchodilator treatment to relieve symptoms in adults with chronic obstructive pulmonary disease (COPD).

COMPLAINT

The complainant alleged that the Evidence Review made an unsubstantiated argument for the treatment of exacerbations. Under a sub-heading on page 6, 'The importance of reducing exacerbations', the second bullet point stated 'Mortality following hospital admission is higher in patients suffering a COPD exacerbation than those with a myocardial infarction at 12 months [Halpin 2008]. The 180 day mortality rate following a COPD exacerbation is 33% [Anzueto 2010] and therefore reductions in exacerbations can reduce mortality rates'.

The complainant stated that the first part of the final sentence was incorrect. The 180 day mortality rate following a COPD exacerbation was not 33%. Anzueto was a review article that highlighted the high mortality rate in a group of patients admitted to hospital with an acute exacerbation of COPD. The paper cited Connors *et al* (1996) which compared outcomes in patients admitted to hospital with an exacerbation of COPD and a Pa_{CO_2} (arterial carbon dioxide tension) of 50mmHg or more (in other words, a particularly ill group of patients with acute hypercapnic respiratory failure). The Evidence Review did not clarify the group of patients to which this data applied. The complainant alleged that the statement was unhelpful and misleading.

More importantly however, was the conclusion of the final sentence 'and therefore reductions in exacerbations can reduce mortality rates'. Whilst the complainant had every desire that this was the case, a thorough literature search showed that this had not been proven. Mortality rates were higher in frequent exacerbators than infrequent exacerbators but the complainant was unaware of any study that had shown that reducing exacerbations with treatments lowered mortality. There was data that suggested that tiotropium might be more effective than long-acting beta agonists (in a study that compared time to first exacerbation of COPD as the primary endpoint, (Vogelmeier *et al* 2011)) but even a four year study in which mortality was a secondary endpoint failed to demonstrate a benefit from the use of tiotropium (Tashkin *et al* 2008).

The complainant further stated that the impact of glycopyrronium on exacerbations was a secondary endpoint in all the trials cited. Although the Evidence Review clarified primary and secondary endpoints, it presented data for a secondary endpoint first. The juxtaposition of the statements on mortality and exacerbations with the secondary endpoint data on exacerbations might lead readers to apply more weight to the information than was supported by evidence.

When writing to Novartis the Authority requested that it consider the requirements of Clauses 7.2, 7.4 and 9.1.

RESPONSE

Novartis submitted that the SUPPORT study (Connors *et al*) referenced by Halpin and Anzueto was selected to illustrate the point about a high (33%) 180 day mortality rate relating to exacerbations. The SUPPORT trial was a high quality, prospective trial with a large trial population, with consequently a large number of exacerbation

events. The patients in the SUPPORT study all had exacerbations leading to hospitalisation and experienced hypercapnoea. Whilst it had been demonstrated that post-exacerbation mortality in patients with hypercapnoea was higher than those with normal ventilation, the impact of severe exacerbation frequency had been demonstrated to have a significantly higher impact on mortality risk compared with the increased risk of mortality relating to hypercapnoea (Soler-Cataluña *et al* 2005).

Another study, the APACHE-III trial (Seneff *et al* 1995) demonstrated that 180 day mortality following an exacerbation which required hospitalisation for patients over 65 years of age was 47%. Therefore the figure quoted in the Evidence Review document at issue indicated that a figure of 33% from the SUPPORT study was not exaggerated and reflective of the incidence of 180 day mortality following hospitalisation.

Seebri Breezhaler was licensed for maintenance bronchodilator treatment of COPD and so the patients in this study would have been within licence. Novartis was therefore confident that it was not necessary to further clarify the group of patients to which these data applied as they were all defined as having COPD. The focus of page 6 charted the potential for progression of COPD as a chronic illness with exacerbations and the improvements for disease management by early intervention. Novartis submitted therefore that this claim represented the available evidence for outcomes of COPD exacerbations and thus it denied a breach of Clauses 7.2 or 7.4.

With regard to the claim 'reductions in exacerbations can reduce mortality rates', Novartis submitted that there was no specific mention of reducing exacerbation rate by any specific treatment at this point in the material at issue. This section was intended to give a brief summary of exacerbations and the impact of exacerbation upon COPD patients and did not make any claims regarding the impact of specific treatments.

It had been well documented that exacerbations had a strong impact on both morbidity and mortality of COPD patients. Halpin specifically stated 'Severe exacerbations of COPD have been shown to be associated with a worse prognosis, and mortality increases with the frequency of exacerbations. Exacerbations of COPD severe enough to require hospitalisation have a significantly greater effect on mortality than those which can be managed in the community'. This was specifically demonstrated by Soler-Cataluña *et al* (2005) which demonstrated that patients with a single unplanned hospital admission had a significantly poorer survival rate than those with no acute exacerbations or COPD or who were not admitted to hospital, and risk of mortality increased with exacerbation frequency to the point where the patients with the greatest mortality risk (of all patient factors considered) were those with three or more acute exacerbations of COPD. Soler-Cataluña *et al* (2009) demonstrated that patients with one or two severe exacerbations had an adjusted mortality risk increased by 2.24-fold, whilst those patients with three or more had an adjusted mortality risk increased by 2.80-fold, thereby demonstrating a clear link between increased exacerbation rate and increased mortality risk. Additionally, Hansel and Barnes (2009) described the impact of exacerbations on disease progression that demonstrated how exacerbations led to accelerated loss of lung function and increasing progression of COPD, which would ultimately lead to increased risk of mortality as the disease progressed. This accelerated decline was specifically illustrated in the paper.

Novartis submitted that other authors had discussed a correlation between reduced exacerbation rates and reductions in mortality: Garcia-Aymerich *et al* (2006) reported that COPD patients with higher than 'very low' physical activity demonstrated a reduction in both hospital admissions and overall mortality risk. Based on this data pulmonary rehabilitation, a frequently used treatment for COPD patients which promoted exercise and prevented further deconditioning, was likely to have a positive effect on exacerbations and therefore mortality. Similarly, a meta-analysis of 22 randomised trials of patients with COPD, Salpeter *et al* (2006) demonstrated that anti-muscarinic compounds demonstrated a reduction in exacerbations of COPD of 33% and a corresponding reduction in mortality of 73% which, despite the potential weaknesses of a small number of the studies in the meta-analysis, clearly highlighted a link between reducing exacerbations and improved mortality.

Novartis stated that scientific and clinical evidence clearly demonstrated that increased numbers of COPD exacerbations increased the overall mortality risk, and there was a clear increase in mortality risk that correlated with the frequency of exacerbations in a year. It thus not only stood to reason but, as stated above, there was data that suggested reducing exacerbation rates could reduce the risk of mortality. Novartis acknowledged, as noted by the complainant, that no single study had successfully demonstrated that a specific treatment for COPD had decreased overall mortality, however, the claim in question did not refer to a specific treatment, and was more a reflection of current medical opinion that reducing exacerbations (using a combination of pharmacological and non-pharmacological treatments and lifestyle changes) led to a significant improvement in the risk of both morbidity and mortality in COPD patients.

Novartis submitted that as the claim reflected current medical opinion in this therapy area and was based on the well established link between exacerbation frequency and mortality rather than the effect on exacerbation frequency of specific treatments, it did not breach Clauses 7.2 or 7.4.

Finally, in response to the complainant's final point of undue weight being given to the exacerbation data from the glycopyrronium studies, it had been clearly stated what the primary and secondary endpoints of the study were, and the reader was not

led into any perception that the exacerbation data was the primary focus of the study. Novartis thus denied a breach of the Code in this regard.

Given the above, Novartis did not consider that it had failed to maintain high standards and it thus denied a breach of Clause 9.1.

PANEL RULING

The Panel noted that the claims at issue appeared as part of the final bullet point on page 6 of the Evidence Review. The claim 'The 180 day mortality rate following a COPD exacerbation is 33%' was referenced to Anzueto, a review of the impact of exacerbations on COPD. The author reviewed, *inter alia*, the impact of exacerbations on mortality and noted that Connors *et al* reported that in patients admitted to hospital with acute hypercapnic respiratory failure, the 180 day mortality rate was 33%. The complainant stated that this was a particularly ill group of patients and that the 180 day mortality rate was not 33%. The complainant had not stated whether he considered the 180 day mortality rate to be more or less than 33%. The Panel noted that Seneff *et al* reported that in a different patient group (those aged 65 years or older admitted to intensive care primarily with an acute exacerbation of COPD), 180 day mortality was 47%. The Panel noted the difference in 180 day mortality rates between the two groups and also that there was no way of comparing the COPD severity of the two groups. The Panel noted Novartis' submission that the 47% 180 day mortality rate in Seneff *et al* indicated that the claim in question was not exaggerated. The Panel noted however that the complaint was not one of exaggeration but of accuracy. Given the difference in the 180 day mortality rate reported in the literature, the Panel considered that the unqualified, unconditional claim at issue 'The 180 day mortality rate following a COPD exacerbation is 33%' was misleading. It implied that the 180 day mortality in any patient following a COPD exacerbation had been categorically proven to be 33% which was not so. In that regard the Panel considered that the claim could not be substantiated. Breaches of Clause 7.2 and 7.4 were ruled.

The Panel noted that the second half of the claim at issue, 'and therefore reductions in exacerbations can reduce mortality rates', was not referenced. Novartis submitted that the claim reflected current medical opinion and was not linked to any specific treatment. The Panel did not accept Novartis' submission that the claim was not linked to any specific treatment. Given the data on the facing page about Seebri Breezhaler and exacerbations there was at the very least an inference that treatment with Seebri Breezhaler would have a positive impact on mortality. The Panel further noted Novartis's submission that no single study had successfully demonstrated that a specific treatment for COPD had decreased overall mortality. Halpin reviewed COPD treatment and noted that although the ISOLDE study showed that inhaled fluticasone significantly reduced the rate of exacerbations, a post hoc analysis only showed a non-significant trend towards improved survival (Briggs *et al* 2006). However, in the TORCH study, although fluticasone reduced the rate of exacerbation, it did not show a reduction in all-cause mortality at 3 years vs placebo (Calverley *et al* 2007). Halpin also reported that tiotropium had been shown to reduce exacerbation frequency and that a post hoc analysis suggested that it might reduce the rate of decline of FEV1; if this was a real effect then it might have an effect on mortality. Halpin further reported the benefits to COPD patients in preventing exacerbations of adding inhaled corticosteroids to long-acting B2-agonists but the studies cited did not link this benefit to a decrease in mortality. Conversely, other studies which examined the impact of adding inhaled corticosteroids to bronchodilator therapy did not link the reduced risk of death with a reduced rate of exacerbation. Halpin acknowledged that the studies reviewed, with the exception of the TORCH study, were not designed to assess mortality rates – most were underpowered as death was an uncommon event. The Panel noted that the complainant had referred to two studies (Tashkin *et al* and Vogelmeier *et al*) neither of which had been cited by Halpin. The complainant noted that these studies showed that although tiotropium was possibly more effective than long-acting B2-agonists, in a study that compared time to first exacerbation of COPD, a four year study in which mortality was a secondary endpoint failed to demonstrate a benefit from the use of tiotropium.

Overall, the Panel considered that although the strong claim that 'reductions in exacerbations can reduce mortality rates' appeared to be self-evident, it did not reflect the balance of the data. The claim implied that reducing COPD exacerbations with treatment had been unequivocally shown to reduce mortality rates which was not so. The Panel considered that the claim was misleading as alleged and could not be substantiated. Breaches of Clauses 7.2 and 7.4 were ruled.

The Panel noted that page 7, which immediately followed and was opposite the claims considered above, was headed 'Glycopyrronium and exacerbations'. The page featured a table which detailed the secondary outcomes from the GLOW-1 study (glycopyrronium vs placebo) and the GLOW-2 study (glycopyrronium vs tiotropium). In both studies the primary efficacy endpoint was trough FEV1 at 12 weeks. Above the table was an explanation that a secondary objective of the two studies was to explore the first COPD exacerbation with glycopyrronium vs placebo over 26 weeks (GLOW-1) and 52 weeks (GLOW-2). Exploratory endpoints for GLOW-2 also included measuring the effect of glycopyrronium vs tiotropium in time to first exacerbation. The table, however, had two columns headed 'Endpoint' and 'Result' and so the secondary nature of the endpoints detailed within was not immediately obvious. The Panel considered that the explanation of the endpoints above the table was not prominent and thus was insufficient in this

regard. The Panel considered that the presentation of the data was not sufficiently complete to allow the reader to appreciate its statistical significance. The Panel considered that the table was misleading in that regard. A breach of Clause 7.2 was ruled.

Given its rulings above, the Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

Complaint received **18 March 2013**

Case completed **1 May 2013**

PHARMACOSMOS/DIRECTOR v VIFOR

Alleged breach of undertaking

Pharmacosmos alleged that a Ferinject (ferric carboxymaltose) advertisement issued by Vifor Pharma breached two previous undertakings. Pharmacosmos marketed Cosmofer (iron dextran). Cosmofer and Ferinject were both indicated for the treatment of iron deficiency when oral preparations were ineffective or could not be used.

As the complaint was about an alleged breach of undertaking it was taken up by the Director as it was the Authority's responsibility to ensure compliance with undertakings.

Pharmacosmos noted that in Case AUTH/2442/10/11 Vifor was ruled in breach of a previous undertaking for continuing to link the dextran shell of Cosmofer to safety concerns by referring to 'dextran-induced hypersensitive reactions' in press releases on the Vifor website. In Case AUTH/2422/7/11, Vifor was ruled in breach for two claims which linked the dextran shell of Cosmofer with safety concerns by highlighting that Vifor was free from 'dextran-induced hypersensitivity reactions since it is free of dextran and dextran derivatives'.

In the advertisement now at issue, Pharmacosmos alleged that the claim 'Non dextran carboxymaltose shell' implied that there was merit to be gained by not being dextran based and that there must be a safety concern with the dextran base and that without it, Ferinject was safer. Pharmacosmos acknowledged that Ferinject did not contain dextran, however it cited certain serious side effects that might occur with the medicine.

The detailed response from Vifor is given below.

The Panel noted that Pharmacosmos had stated that Vifor had been previously ruled in breach of the Code because of claims which raised safety concerns about the dextran shell of Cosmofer. This was not so. In Case AUTH/2422/7/11 the Panel upheld Pharmacosmos's allegation that the claim 'Ferinject avoids dextran-induced hypersensitive reactions' was misleading about Ferinject itself; the ruling was not made on the basis that the claim raised concerns about Cosmofer. Similarly in Case AUTH/2442/10/11, Pharmacosmos had referred to claims which had wrongly implied that Ferinject was free of hypersensitivity reactions.

The Panel noted that neither the claim now at issue, 'Non dextran carboxymaltose shell' nor the other two bullet points in the advertisement ('Effective in increasing haemoglobin when inflammation is present' and '1000mg can be administered in 15 minutes by IV injection and IV infusion') referred to hypersensitivity reactions. In the Panel's view, neither the claim of itself nor the advertisement sought to minimise concerns about such reactions with Ferinject. The Panel did not consider that the claim was covered by the previous undertakings and thus it ruled no breach of the Code including no breach of Clause 2.

Pharmacosmos A/S alleged that a Ferinject (ferric carboxymaltose) advertisement (ref UK/FER/12/0163c), issued by Vifor Pharma UK and published in Gastrointestinal Nursing, January 2013, breached the undertakings given in Cases AUTH/2422/7/11 and AUTH/2442/10/11. The advertisement at issue featured the photograph of a leaping ballerina together with three bullet points, the second of which read 'Non dextran carboxymaltose shell'.

Pharmacosmos marketed Cosmofer (iron dextran). Cosmofer and Ferinject were both indicated for the treatment of iron deficiency when oral preparations were ineffective or could not be used.

As the complaint was about an alleged breach of undertaking it was taken up by the Director as it was the Authority's responsibility to ensure compliance with undertakings.

COMPLAINT

Pharmacosmos alleged that the claim 'Non dextran carboxymaltose shell' was the latest attempt by Vifor to use the molecular structure as a differentiating safety feature between Ferinject and Cosmofer which was a dextran-based molecule.

Pharmacosmos noted that in Case AUTH/2442/10/11 Vifor was ruled in breach of Clause 25 for continuing to link the dextran shell of Cosmofer to safety concerns by referring to 'dextran-induced hypersensitive reactions' in press releases on the Vifor website. In Case AUTH/2422/7/11, Vifor was ruled in breach of Clause 7.2 for two claims which linked the dextran shell of Cosmofer with safety concerns by highlighting that Vifor was free from 'dextran-induced hypersensitivity reactions since it is free of dextran and dextran derivatives'.

Pharmacosmos considered that the advertisement now at issue continued to imply that there was merit to be gained by not being dextran based. The only reasonable conclusion that physicians could draw from the bullet point was that there must be a safety concern with the dextran base and therefore leaving it out must mean that Ferinject was safer. Pharmacosmos acknowledged that Ferinject did not contain dextran, however it cited certain serious side effects that might occur with the medicine. These risks must be mentioned if albeit indirectly referring to the safety of competing products in promotional material. Pharmacosmos referred to a recent Rapporteur report to the European Medicines Agency (EMA).

Pharmacosmos alleged that the claim was a continuation of the previous attempts to raise concerns about the safety profile of the dextran molecule in Cosmofer, in breach of the undertakings given in Cases AUTH/2442/10/11 and AUTH/2422/7/11.

When writing to Vifor, the Authority asked it to respond in relation to the requirements of Clause 2 in addition to Clause 25 cited by Pharmacosmos.

RESPONSE

Vifor stated that it was committed to adhering to the Code and that it took allegations of a breach of undertaking extremely seriously. However, Pharmacosmos had raised new and additional concerns that fell outside the undertakings previously given and, as such, there was no automatic right to circumvent the complaints process. The undertakings in Cases AUTH/2442/10/11 and AUTH/2422/7/11 referred to the claim 'Ferinject avoids dextran-induced hypersensitivity reactions' which was ruled in breach of the Code because it was misleading about the safety of Ferinject. Vifor noted that Pharmacosmos had now alleged that the claim 'non dextran carboxymaltose shell' was a breach of those undertakings. This was a new complaint. Vifor submitted that where new complaints arose that did not fall under a breach of Clause 25, Paragraph 5.3 of the Constitution and Procedure required inter-company dialogue first, ie 'that the company concerned has previously informed the company alleged to have breached the Code that it proposed to make a formal complaint and offered inter-company dialogue at a senior level in an attempt to resolve the matter, but that this offer was refused or dialogue proved unsuccessful'. Vifor stated that Pharmacosmos had made no such offer and Vifor viewed this as an abuse of process.

Following the ruling of a breach in Case AUTH/2422/7/11, almost all of the promotional material used by the sales teams was withdrawn. Additionally, all the materials held by the sales teams were collected and destroyed. As a consequence of the breach, a comprehensive internal review was undertaken and all material along with internal approval and material withdrawal processes were reviewed. Two press releases which were prepared globally were not part of this review, a regrettable oversight by Vifor that resulted in Case AUTH/2442/10/11. Following the second case, the boiler plate which contained the claim at issue provided by Vifor Pharma International was replaced and an additional step was added into the standard operating procedure (SOP) for material withdrawal to ensure this did not happen again. Vifor reiterated that all material was now rigorously reviewed before release.

With regard to the claim now at issue, Vifor considered that 'Non dextran carboxymaltose shell' was not about the safety of Ferinject but about its physiochemical properties, completely in line with Section 4.2 of the Ferinject summary of product characteristics (SPC), which allowed up to 1000mg of Ferinject to be administered in 15 minutes. The claim referred exclusively to the physiochemical properties of Ferinject and linked that to its administration according to its SPC. There was no direct or indirect reference to any safety aspects of Cosmofer or, indeed, any other product. Neither the claim in question nor the advertisement referred (directly or indirectly) to safety, adverse events or hypersensitivity reactions, dextran-induced or not (dextran-induced hypersensitivity reaction was the subject of the previous undertakings). As stated above, Vifor did not consider that there was a breach of undertaking and consequently there was no breach of Clauses 25 or 2. The claim was simply about the physiochemical properties of Ferinject rather than its safety.

Vifor was particularly concerned that Pharmacosmos had referred to an EMA report. While it was public knowledge that a Europe wide review of all intravenous iron preparations was in progress, the contents of interim reports generated as part of that process were not. Disclosure of the EMA's preliminary documents was a clear breach of trust within the context of the EMA's referral procedure, where all parties involved (EMA, Rapporteurs, marketing authorization holders, experts) must be able to exchange preliminary views without fear of those views being disclosed prior to the final decision. The EMA clearly recognised that publication of reports should occur only once the final opinion had been adopted. Disclosure of such preliminary documents before a final decision was made had potential serious public health consequences.

Vifor was extremely concerned that Pharmacosmos' intention was to manipulate the complaints process to ensure that an out of context element of a confidential, preliminary EMA statement was included in the case report with the specific intent of making this selective incomplete information public.

In summary, Vifor strenuously denied a breach of Clause 25 and hence Clause 2, based on the narrow, tenuous and misleading points raised and considered that the complaints process had been abused by Pharmacosmos.

PANEL RULING

The Panel noted that in Case AUTH/2422/7/11 the material at issue had been a leavepiece which in a section headed 'How quickly can Ferinject be administered?', featured the claim 'Ferinject avoids dextran-induced hypersensitive reactions'. In Case AUTH/2422/7/11 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.

The Panel did not accept Vifor's submission in Case AUTH/2422/7/11 that the potential for hypersensitivity reactions with Ferinject *per se* was a separate issue. In the Panel's view, the claim 'Ferinject avoids dextran-induced hypersensitive reactions' 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 of Clause 7.2 was ruled which was accepted by Vifor.

Case AUTH/2442/10/11 involved two press releases. The Panel considered that the claim in one of the press releases '…not associated with dextran-induced hypersensitivity reactions' was covered by the undertaking in Case AUTH/2422/7/11. 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 concerns about such reactions. A breach of Clause 25 was ruled as acknowledged by Vifor.

Although the claim in the other press release that Ferinject was '…not associated with dextran-induced hypersensitivity reactions since it is free of dextran and dextran derivatives…' gave more details it again implied that there was no need to be concerned about hypersensitivity reactions with Ferinject. In the Panel's view this was similarly covered by the undertaking in Case AUTH/2422/7/11. A further breach of Clause 25 was ruled as acknowledged by Vifor.

The Panel noted that in the case now at issue, Case AUTH/2589/3/13, Pharmacosmos had stated that Vifor had been previously ruled in breach of the Code because of claims which raised safety concerns about the dextran shell of Cosmofer. This was not so. In Case AUTH/2422/7/11 Pharmacosmos had alleged that the claim 'Ferinject avoids dextran-induced hypersensitive reactions' was misleading about Ferinject itself; not that it raised concerns about Cosmofer. Similarly in Case AUTH/2442/10/11, Pharmacosmos had referred to claims which had wrongly implied that Ferinject was free of hypersensitivity reactions.

The Panel noted that neither the claim now at issue, 'Non dextran carboxymaltose shell' nor the other two bullet points in the advertisement ('Effective in increasing haemoglobin when inflammation is present' and '1000mg can be administered in 15 minutes by IV injection and IV infusion') referred to hypersensitivity reactions. In the Panel's view, neither the claim of itself nor the advertisement as a whole sought to minimise concerns about such reactions with Ferinject. The Panel did not consider that the claim was covered by the previous undertakings and thus it ruled no breach of Clause 25. Given its ruling of no breach of Clause 25, the Panel subsequently ruled no breach of Clause 2.

Complaint received **25 March 2013**

Case completed **24 April 2013**

CASE AUTH/2591/3/13

ANONYMOUS v MERCK SERONO

Conduct of representative

An anonymous, non-contactable complainant, complained about the conduct of an un-named representative from Merck Serono who had requested a monthly visit throughout 2013. The complainant stated that he/she felt harassed as such frequent meetings were unnecessary. The complainant was informed that these visits were required to meet an instruction to have meetings with seven health professionals each day.

The complainant noted that before this episode, he/she had always found the representative to be very professional and an asset to the company. The complainant considered that the representatives were being forced to behave in this way by unrealistic expectations from their managers.

The detailed response from Merck Serono is given below.

The Panel noted that Merck Serono's instructions to its representatives referred to a number of different targets. For example, representatives were to see 90% of their colorectal cancer (CRC) oncologists at least 3 times per year. An additional incentive was paid to representatives who saw 20 CRC oncologists in the next 10 working days. Gold, Silver and Bronze targets were set in the Erbitux campaign brief 2013 and the minimum standard was to aim to see 2 gold contacts a day and five others from the silver and bronze contact list. According to the complainant it appeared that this instruction was referred to by the representative. The objectives referred to seeing a 'minimum' of three per year. None of the materials which instructed the representatives referred to the Code requirements concerning call rates or distinguished between call rates and contact rates. The email Merck Serono sent following the complaint referred to the expectations in the representatives' objectives and that 'for the avoidance of doubt there must not be any more than 3 unsolicited meetings with any one HCP over the year'. In addition, the Panel noted that following the complaint the Erbitux campaign brief which set the targets had been withdrawn.

The Panel ruled a breach as Merck Serono's instructions to representatives advocated a course of action which was likely to breach the Code. The Panel noted that the Code also required representatives to ensure that, *inter alia*, the frequency of their calls on health professionals did not cause inconvenience and supplementary information which stated that the number of calls should not normally exceed 3 on average. No evidence had been submitted to establish whether a breach of this clause had occurred. The complainant was non contactable, thus the Panel could not seek further information. No breach of the Code was ruled.

An anonymous, non-contactable complainant, complained about the conduct of an un-named representative from Merck Serono.

COMPLAINT

The complainant was concerned about a meeting that he/she had had with a Merck Serono representative. The complainant alleged that the representative had requested that he/she plan a monthly visit with him/her throughout 2013. The complainant stated that he/she felt harassed by this request as such frequent meetings were completely unnecessary. When the complainant asked why the representative wanted to plan so many meetings in advance he/she was informed that these visits were required to meet an instruction to have meetings with seven health professionals each day.

The complainant noted that before this episode, he/she had always found this representative to be very professional and an asset to his/her company. The complainant considered that the representatives were being forced to behave in this way by unrealistic expectations from their managers.

The complainant stated that he/she had complained anonymously as Merck Serono had always been very supportive to his/her department and he/she did not wish to get the representative into trouble.

When writing to Merck Serono the Authority asked it to respond in relation to Clauses 15.4 and 15.9 of the Code.

RESPONSE

Merck Serono operated three field forces, one promoting Rebif (interferon-beta 1alpha) and Saizen (recombinant growth hormone), one promoting Erbitux (cetuximab) and one promoting a range of fertility products.

Merck Serono's philosophy was that the quality of the interaction with health professionals was more important than quantity and therefore there was not an emphasis on call rates.

The Rebif, Saizen and fertility materials made no mention of call or contact rates.

Merck Serono stated that the most recent oncology material contained the phrase 'Selling the OS [overall survival] message to a minimum of 90% of your CRC [colorectal cancer] Oncologists at least three times per year' and a short term incentive – '20 in 10' – to see 20 CRC oncologists in the next 10 working days. A copy of the meeting slides was provided. This wording reflected an item in representative's annual objectives regarding contact rates:

'Coverage and frequency on CRC Oncologists and Liver Surgeons

To see 90% of CRC Oncologists and Liver Surgeons a minimum of 3 x per year to communicate the key messages and thus drive sales of Erbitux.'

This was followed by various targets for seeing clinicians 'a minimum of 3 x per year'.

Merck Serono submitted that as these contacts included meetings, solicited as well as unsolicited calls, these objectives complied with the Code and did not breach Clauses 15.4 or 15.9.

Merck Serono provided the Erbitux Campaign brief 2013. There were additional instructions for Q1 2013 'As a minimum standard you should be aiming for 2 Gold contacts per day and 5 others from your silver and bronze contact lists'. This seemed to form the basis for the representative's actions. The number of Gold, Silver and Bronze targets per representative was provided.

Merck Serono stated that representatives were in the field an average of four days a week. If they were to achieve this standard through meetings, solicited as well as unsolicited calls an activity level of eight Gold customers and twenty Silver and Bronze customers would be required per representative per week. The majority of contacts in colorectal cancer were the result of either pre-arranged meetings or follow-up activity. It was therefore very unlikely that there would be any risk of some customers being seen with undue frequency. Merck Serono submitted that management expectations were not at all unrealistic as alleged by the complainant.

The instruction to see two Gold and five Silver and Bronze targets per day had not been enforced and was not linked to any metric or financial incentive. As a result of this complaint an email had been sent to the representatives clarifying that this particular instruction was subject to Code compliance and that no more than three unsolicited calls per year were to be made. The focus should be on the coverage given in the latest briefing in March. To avoid a potential misinterpretation the campaign brief had been withdrawn. A copy of this email was provided together with the sales manager's monthly emails to the field force from Q1 2013 which did not mention call rates.

Merck Serono submitted that the representative in question confused the two contact rates in making the request. Merck Serono had taken the actions outlined above and would issue further written instructions to reinforce that call frequency was to remain compliant with the Code. It very much regretted the conduct of the representative in this case but submitted this was an individual aberration and did not reflect the normal standard demonstrated by Merck Serono representatives.

PANEL RULING

The Panel noted that the complainant was anonymous and non contactable. Like all complaints, anonymous complaints were judged on the evidence. The complainant had the burden of proving their complaint on the balance of probabilities.

The Panel noted that the supplementary information to Clause 15.4 Frequency and Manner of calls on Doctors and other Prescribers 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 the requirements of Clause 15.9 included that briefing material must not advocate either directly or indirectly any course of action which would be likely to lead to a breach of the Code.

The Panel noted that Merck Serono's instructions to its representatives referred to a number of different targets. For example, representatives were to see 90% of their CRC oncologists at least 3 times per year. An additional incentive of £250 in vouchers was paid to representatives who saw 20 CRC oncologists in the next 10 working days. Gold, Silver and Bronze targets were set in the Erbitux campaign brief 2013 and the minimum standard was to aim to see two gold contacts a day and five others from the silver and bronze contact list. According to the complainant it appeared that this instruction was referred to by the representative. The objectives referred to seeing a 'minimum' of three per year. None of the materials which instructed the Merck Serono representatives referred to the Code requirements concerning call rates or distinguished between call rates and contact rates. The email Merck Serono sent following the complaint referred to the expectations in the representatives' objectives and that 'for the avoidance of doubt there must not be any more than 3 unsolicited meetings with any one HCP over the year'. In addition, the Panel noted that following the complaint the Erbitux campaign brief which set the Gold, Silver and Bronze targets had been withdrawn.

The Panel considered that Merck Serono's instructions to representatives 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 and its

supplementary information required that the number of calls should not normally exceed 3 on average. No evidence had been submitted to establish whether a breach of this clause had occurred. Whilst according to the complainant the representative had requested monthly visits there was no evidence that the complainant had agreed to this request or that the meetings had otherwise occurred. The complainant was non contactable, thus the Panel could not seek further information. No breach of Clause 15.4 was ruled.

Complaint received **26 March 2013**

Case completed **2 May 2013**

CASE AUTH/2592/4/13

VOLUNTARY ADMISSION BY GLAXOSMITHKLINE

Benlysta case studies

GlaxoSmithKline voluntarily admitted that two promotional case studies for Benlysta (belimumab), were emailed to health professionals without being certified. Benlysta was indicated as add-on therapy in adults with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity despite standard therapy.

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

GlaxoSmithKline explained that some of the information provided in the case studies was inconsistent with the Benlysta summary of product characteristics (SPC) and the link to the prescribing information did not work. However, the prescribing information could be accessed through the link to the product website. The company immediately recalled the non-compliant emails and investigated the events surrounding this error.

The detailed response from GlaxoSmithKline is given below.

The Panel noted that two case studies which promoted the use of Benlysta were emailed as a 'Dear Doctor' letter to health professionals prior to certification. The Panel acknowledged that as soon as GlaxoSmithKline became aware of the problem, it emailed the recipients to recall the information and to alert them that some of the information (ie the case study in the lupus nephritis class IV patient) might have been inconsistent with the Benlysta SPC. The recall email stated that Benlysta had not been studied in, and was not recommended in, *inter alia*, severe active lupus nephritis. The relevant part of the SPC was reproduced. Recipients were asked to acknowledge receipt of the recall email. The Panel noted with concern that recipients were not asked to delete the original 'Dear Doctor' letters.

The Panel noted that the letters were promotional and had not been certified. A breach of the Code was ruled. The emailed letters did not include the Benlysta prescribing information and the prescribing information link was not active. Although recipients could access the prescribing information via a link to the product website, the Panel did not consider that this was acceptable; prescribing information should be provided as an integral part of promotional material and should not be separate from it. The emails were 'Dear Doctor' letters sent electronically. A breach of the Code was ruled.

The Panel noted that according to its SPC, Benlysta had not been studied in, and was not recommended in severe active lupus nephritis. One of the case studies was of a patient who had lupus nephritis class IV in renal biopsy. The Panel noted that the clinician who had submitted the case study confirmed that in his/her opinion this patient was classed as having severe active lupus nephritis. The Panel thus considered the case study promoted the use of Benlysta in a manner which was inconsistent with the particulars listed in its SPC and was misleading in that regard. Breaches of the Code were ruled.

GlaxoSmithKline UK Limited voluntarily admitted that two promotional case studies for Benlysta (belimumab), were emailed to health professionals without being certified. Benlysta was indicated as add-on therapy in adults with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity despite standard therapy.

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

COMPLAINT

GlaxoSmithKline stated that the breaches related to two Benlysta case studies that were sent to health professionals in error before they had gone through the company's standard review process for promotional materials.

The case studies were from a health professional who used Benlysta and were submitted to head office by a commercial manager to go through the promotional material approval process. The case studies were in email format. The purpose of the case studies was, in the anticipation of the final National Institute for Health and Care Excellence (NICE) guideline, to inform other lupus specialists of an important although limited experience with the product. Health professionals were encouraged to share their experience with GlaxoSmithKline in the first instance, which would be shared with other health professionals in accordance with the requirements of the Code.

Another member of the business unit team was responsible for raising new case study items in Zinc (GlaxoSmithKline's electronic system for approval of promotional materials). The case studies were duly added to Zinc to start the approval process.

There was a lag of two weeks from the case studies being submitted to head office and the new items being raised in Zinc. An email was sent to the commercial manager to confirm that the items had been raised in Zinc; the email stated the reference codes for the items and confirmed that they were awaiting review. The commercial manager mistakenly thought that the items had been approved and, forwarded the two unapproved

case studies to 48 health professionals (who had previously agreed to receive promotional emails). Members of the GlaxoSmithKline commercial business unit and medical team were blind copied on the emails.

Three days later a medical advisor and ABPI signatory returned from leave and realised that the case study emails had not been reviewed and approved. Further that some of the information provided in the case studies was inconsistent with the Benlysta summary of product characteristics (SPC) and that the link to the prescribing information did not work. However, the prescribing information could be accessed through the link to the product website. The matter was reported to the medical director who instigated an immediate recall of the non-compliant emails and an investigation into the error.

A commercial manager subsequently issued an email to recall the unapproved patient case studies, explained the essence of the error and asked recipients to confirm receipt of the recall email. In addition, the recall email contained a corrective statement with regard to the approved label as per the SPC.

Of the 48 recipients, 3 were returned undelivered which left 45 to be followed up. Two days prior to the submission of the voluntary admission 44 out of 45 confirmations had been received. The non-responder was being followed up for documented evidence acknowledging the receipt of recall.

GlaxoSmithKline submitted that the following further corrective actions were in process;

1 Ensuring that the health professional who had not yet responded confirmed receipt of the recall message.
2 Re-training the commercial manager on the approval process.
3 Production of a case study for sharing with the broader organisation to ensure that lessons were learnt from this error.
4 Initiation of a specific audit to review release of materials following certification.

GlaxoSmithKline submitted that this was an administrative error which led to the circulation of unapproved promotional case studies. GlaxoSmithKline was confident that this was an isolated incident.

GlaxoSmithKline stated that it took its obligations to comply with the Code seriously and was committed to ensuring that all staff were appropriately trained and acted in compliance with the Code.

When writing to GlaxoSmithKline the Authority asked it to consider the requirements of Clauses 3.2, 4.1, 7.2 and 14.1.

RESPONSE

GlaxoSmithKline explained that Benlysta was indicated as add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (eg positive anti-dsDNA and low complement) despite standard therapy. Section 4.4 of the SPC, Special Warnings and Precautions for Use, stated that Benlysta had not been studied in a number of patient groups, and was not recommended, *inter alia*, in severe active lupus nephritis.

GlaxoSmithKline noted that one of the case studies was that of a 35 year old female. In the section entitled 'symptoms/disease activity' the description was 'Lupus nephritis class IV on renal biopsy'. With regard to Clause 3.2, the sender of the email had not appreciated that this might be interpreted as one of the conditions listed in Section 4.4 of the SPC. GlaxoSmithKline had contacted the treating clinician who had confirmed that in his/her opinion this patient was classed as having severe active lupus nephritis. The clinician and the team involved knew the limitations of the licence and had made a clinical decision to prescribe.

With regard to Clause 7.2, GlaxoSmithKline submitted that the information contained in the email was accurate, fair and balanced.

Details of the product website landing page at the time the emails were sent were provided.

GlaxoSmithKline reiterated that although a link to the Benlysta prescribing information was not active the email included an active link to the Benlysta website hosted on the health professional part of health.gsk.co.uk, a promotional website with current prescribing information, therefore recipients would have been able to access the prescribing information from the email. A screen shot of the home page the reader was directed to on confirmation that they were a health professional, and the prescribing information which was active when the email was sent, were provided.

PANEL RULING

The Panel noted that the two case studies which promoted the use of Benlysta were emailed as a 'Dear Doctor' letter to health professionals prior to certification. The Panel acknowledged that as soon as GlaxoSmithKline became aware of the problem, it emailed the recipients of the case studies to recall the information and to alert them that some of the information (ie the case study in the lupus nephritis class IV patient) might have been inconsistent with the Benlysta SPC. It was noted in the recall email that Benlysta had not been studied in, and was not recommended in, *inter alia*, severe active lupus nephritis. The relevant part of the SPC was reproduced. Recipients were asked to acknowledge receipt of the recall email. The Panel noted with concern that recipients had not been asked to delete the original 'Dear Doctor' letters.

The Panel noted that the letters were promotional and had not been certified. A breach of Clause 14.1 was ruled. The emailed letters did not include the Benlysta prescribing information. In addition, the Panel noted that the prescribing information link was not active. Although the Panel noted

GlaxoSmithKline's submission that recipients could access the prescribing information via a link to the product website, it did not consider that this was acceptable; prescribing information should be provided as an integral part of promotional material and should not be separate from it. The emails were 'Dear Doctor' letters sent electronically. A breach of Clause 4.1 was ruled.

The Panel noted that Section 4.4 of the Benlysta SPC stated that Benlysta had not been studied in, and was not recommended in, *inter alia*, severe active lupus nephritis. One of the case studies sent to health professionals was of a patient who had lupus nephritis class IV in renal biopsy. The Panel noted that the clinician who had submitted the case study confirmed that in his/her opinion this patient was classed as having severe active lupus nephritis. The Panel thus considered the case study promoted the use of Benlysta in a manner which was inconsistent with the particulars listed in its SPC and was misleading in that regard. Breaches of Clauses 3.2 and 7.2 were ruled.

Complaint received **11 April 2013**

Case completed **14 May 2013**

GENERAL PRACTITIONER v LUNDBECK

Email promotion of Cipralex

A general practitioner complained about an unsolicited Cipralex (escitalopram) email which he had received from a database agency on behalf of Lundbeck.

The complainant stated that he did not usually receive direct marketing about medicines and queried whether the email at issue was a spam email.

The detailed response from Lundbeck is given below.

The Panel noted that the Code prohibited the use of email for promotional purposes except with the prior permission of the recipient. Whilst the material at issue had not been sent directly by Lundbeck it was nonetheless an established principle under the Code that pharmaceutical companies were responsible for work undertaken by third parties on their behalf.

The Panel noted that when obtaining permission from health professionals to add them to their database, [and thus contact them through their NHS email account] the database agency had made it clear to them that it would, from time to time, email information which might include, inter alia, pharmaceutical promotional material. The Panel noted Lundbeck's submission that the complainant had been on the database since 2007 and that the complainant's details had been verified within the last year.

The Panel noted that the unsubscribe facility linked to the email in question appeared to enable a recipient to unsubscribe to all Lundbeck emails but not to promotional emails from any other company sent by the database agency. Opting in to receive promotional emails appeared to allow the database agency to send material from any pharmaceutical company; it seemed that opting out, however, had to be done company by company. The Panel queried whether this was entirely consistent with the Code. Nonetheless, on the material available, it appeared that on registration and on the last annual verification of his details, the complainant had agreed to receive pharmaceutical promotional material by email. The Panel consequently ruled no breach of the Code.

A general practitioner complained about an unsolicited Cipralex (escitalopram) email (ref UK/ESC/1303/0400) which he had received in April 2013 from an electronic marketing agency on behalf of Lundbeck Limited.

COMPLAINT

The complainant stated that the company and its sister company, seemed a bit fishy/spammy and hence the query about whether the email was in breach of the Code. The complainant stated that he did not usually receive direct marketing about medicines.

When writing to Lundbeck the Authority asked it to respond in relation to Clause 9.9 of the Code.

RESPONSE

Lundbeck stated that it had developed the Cipralex email in conjunction with a digital agency. That agency worked directly with an electronic marketing agency which owned a database of health professionals.

The electronic marketing agency sent the email only to health professionals that had registered on the database and had agreed to receive promotional emails from pharmaceutical companies. Lundbeck requested that the health professionals that would be interested in receiving the Cipralex email would be registered GPs and psychiatrists only who had opted in to receive promotional emails.

The database included medical professionals employed within the NHS and UK private healthcare sector. Registered users had free access to information on the site, including information about prescription only medicines and medical devices, which could only be directed and accessed by health professionals who prescribed these products.

The complainant was first approached by the database in 2007 and had been a member since then and his registration was last verified in September 2012. Lundbeck provided a set of slides which explained the registration process.

An electronic marketing agency initially approached the complainant by telephone. This conversation included background information on the services provided, and specifically referred to the potential use of email for pharmaceutical promotional materials:

> '[the agency] will from time to time send information by e-mail about our associated/affiliated companies and their clients' product and services, which may include updates on specialist services, conferences and seminars, diagnostic, medical and pharmaceutical promotional materials as well as official information.'

A confirmation email was then sent to the complainant which included the text reproduced above and the opportunity to opt out. The complainant completed his registration on the 1 June 2007 and opted in to receive promotional emails.

Registered users of the database were contacted annually to check that their contact details were up-to-date and that they wished to continue their membership. They were emailed with the text quoted above and had to acknowledge their wish to opt in to continue receiving promotional emails.

Promotional emails, including the Cipralex email at issue, included an option to opt out of receiving further emails. When a health professional clicked the 'opt out' link at the bottom of the email, they were taken to an automated email which was sent directly to an electronic marketing agency's data department. The following steps were then taken:

- Unique identifier identified the health professional to allow extraction from the database
- The record was placed in the unsubscribed holding file
- The health professional was unsubscribed to all emails from that company, regardless of therapy area.

The complainant elected to receive promotional emails and had not opted out, despite clear opportunities to do so. Lundbeck did not consider the email at issue was unsolicited, and it believed that all the requirements of Clause 9.9 had been fulfilled. Of course, if the complainant did not wish to receive promotional emails Lundbeck would ensure that he was unsubscribed.

PANEL RULING

The Panel noted that Clause 9.9 prohibited the use of email for promotional purposes except with the prior permission of the recipient. The Panel considered that the email in question was clearly promotional material. Whilst it had not been sent directly by Lundbeck it was nonetheless an established principle under the Code that pharmaceutical companies were responsible for work undertaken by third parties on their behalf. The email stated in small font at the end that it had been forwarded by an electronic marketing agency on behalf of Lundbeck. This was followed by a link which would allow the recipient to unsubscribe, although it appeared that following the link might only stop future Lundbeck emails.

The Panel noted that when obtaining permission from health professionals to add them to their database, the database agency had made it clear that it would, from time to time, email information about associated/affiliated companies, and their clients' products and services which might include updates on specialist services, conferences and seminars, diagnostic, medical and pharmaceutical promotional materials as well as official information. The Panel noted the company's submission that the database organisation had first approached the complainant by telephone and had referred to the use of email for pharmaceutical company materials. This was followed by a registration email on 31 May 2007 which again made it clear that the company intended to email promotional material from pharmaceutical companies. Lundbeck submitted that the complainant's details were verified annually and had last been verified by email in September 2012. A copy of this email which referred to the provision of pharmaceutical promotional materials had been provided.

The Panel noted that the unsubscribe facility linked to the email in question appeared to enable a recipient to unsubscribe to all Lundbeck emails but not to promotional emails from any other company sent by the database agency. Opting in to receive promotional emails appeared to allow the database agency to send material from any pharmaceutical company; it seemed that opting out, however, had to be done company by company. The Panel queried whether this was entirely consistent with the supplementary information to Clause 9.9 which stated that where permission to use emails for promotional purposes has been given to a recipient, each email sent should inform the recipient how to unsubscribe to them. Nonetheless, on the material available, it appeared that on registration and on the last annual verification of his details, the complainant had agreed to receive pharmaceutical promotional material by email. The Panel consequently ruled no breach of Clause 9.9.

Complaint received **12 April 2013**

Case completed **4 June 2013**

CASE AUTH/2595/4/13

PHARMACIST v LILLY

Promotion of Alimta

A pharmacist member of a cancer services network complained about a 'Dear Doctor' letter sent by Eli Lilly and Company which referred to Alimta (pemetrexed) continuation maintenance now being listed with funding available from the National Cancer Drugs Fund for patients with non-squamous non small cell lung cancer (NS NSCL).

The complainant drew attention to the second part of the letter that 'The Paramount trial demonstrated that Alimta continuation maintenance treatment plus best supportive care (BSC) versus placebo plus BSC immediately following induction with Alimta/ cisplatin for advanced NS NSCLC showed a *median overall survival of 16.9 months* with a manageable side effect profile'.

The complainant alleged a breach of the Code as the letter, by not referring to the survival of the placebo group, implied that pemetrexed added 16.9 months survival advantage. The claim of 16.9 months was from induction rather than the 13.9 months that was quoted in the summary of product characteristics (SPC) which was from the start of maintenance treatment.

The detailed response from Lilly is given below.

The Panel noted that the Paramount study showed a survival benefit for pemetrexed maintenance therapy vs placebo (median overall survival 16.9 months vs 14 months respectively) from the start of induction treatment. The 'Dear Doctor' letter, however, only referred to the pemetrexed results and did not give the results for the placebo group. In that regard the Panel did not consider that the letter was sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of pemetrexed. The letter was misleading in that regard and a breach was ruled.

The Panel further noted that the letter referred to the 'median overall survival of 16.9 months' demonstrated with pemetrexed but only the phrase 'overall survival of 16.9 months' was emboldened; the preceding 'median' was in normal typeface. The Panel considered that the emphasis on 'overall survival of 16.9 months' was such that the letter was misleading and not capable of substantiation. Further breaches were ruled.

In the Panel's view, it was likely that some readers would assume that 'immediately following induction' with Alimta/cisplatin as used in the letter, was the same as 'Following Alimta plus cisplatin induction' as used in the SPC. This was not so. The Panel considered that the letter was not entirely clear from which time point the 16.9 months survival had been measured and a breach was ruled.

A pharmacist member of a cancer services network complained about a 'Dear Doctor' letter (ref UKALM00536a) from Eli Lilly and Company Limited. The letter referred to Alimta (pemetrexed) continuation maintenance now being listed with funding available from the National Cancer Drugs Fund for patients in England with non-squamous non small cell lung cancer (NS NSCL).

COMPLAINT

The complainant drew attention to the second part of the letter that:

> 'The Paramount trial demonstrated that Alimta continuation maintenance treatment plus best supportive care (BSC) versus placebo plus BSC immediately following induction with Alimta/ cisplatin for advanced NS NSCLC showed a median **overall survival of 16.9 months** with a manageable side effect profile.'

The complainant alleged that the above was in breach of Clause 7 of the Code as it implied that pemetrexed added 16.9 months survival advantage, as it did not refer to the survival of the placebo group.

The claim of 16.9 months was from induction rather than the 13.9 months that was quoted in the summary of product characteristics (SPC) which was from the start of maintenance treatment.

When writing to Lilly, the Authority asked it to respond in relation to Clauses 7.2 and 7.4.

RESPONSE

Lilly stated that the PARAMOUNT registration trial assessed the superiority of pemetrexed as continuation maintenance treatment compared with placebo after induction treatment with pemetrexed and cisplatin for patients with advanced non-squamous non small cell lung cancer.

Eligible patients (n=939) received 4 cycles of induction treatment with pemetrexed and cisplatin. Patients who showed clinical response were then randomised to receive either pemetrexed plus best supportive care (BSC) maintenance treatment (n=359) or placebo plus BSC (n=180). The median overall survival (mOS) from randomisation (start of continuation maintenance) was 13.9 months for patients in the pemetrexed arm, compared with 11 months for the placebo group (p=0.0195, unadjusted HR=0.78, 95%CI:0.64-0.96). For patients who received both induction and maintenance, the mOS from the start of induction treatment was 16.9 months for pemetrexed vs 14 months for placebo (P=0.0191, HR=0.78, 95% CI:0.64-0.96). The values for

mOS from induction included both non-randomised and randomised components.

The 'Dear Doctor' letter at issue referred to 16.9 months as the 'median overall survival' for patients participating in PARAMOUNT.

Further, the letter was primarily intended to notify health professionals that pemetrexed as a continuation maintenance treatment option for patients with advanced NS NSCLC could be funded through the National Cancer Drugs Fund. There was no intention to mislead health professionals about the PARAMOUNT data. However, Lilly agreed that additional data points as published in the study report and SPC should have been included for completeness. Accordingly, Lilly withdrew the letter with immediate effect on 18 April, the day it received notice of the complaint. The letter had been replaced with a new version containing additional data points.

With regard to the complainant's view that the claim of 16.9 months was from induction rather than the 13.9 months that was quoted in the SPC which was from the start of the maintenance treatment, Lilly noted that both the figures relating to mOS could be found in Section 5.1 of the SPC. This claim could therefore be substantiated and Lilly denied a breach of Clause 7.4.

PANEL RULING

The Panel noted that the Paramount study showed a survival benefit for pemetrexed maintenance therapy vs placebo (median overall survival 16.9 months vs 14 months respectively) from the start of induction treatment. The 'Dear Doctor' letter, however, only referred to the pemetrexed results and did not give the results for the placebo group. In that regard the Panel did not consider that the letter was sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of pemetrexed. The Panel considered that the letter was misleading in that regard and a breach of Clause 7.2 was ruled.

The Panel further noted that the 'Dear Doctor' letter referred to the 'median overall survival of 16.9 months' demonstrated with pemetrexed but only the phrase 'overall survival of 16.9 months' was emboldened; the preceding 'median' was in normal typeface. The Panel considered that the emphasis on 'overall survival of 16.9 months' was such that the letter was misleading in that regard and a further breach of Clause 7.2 was ruled. The Panel considered that the selective emboldening of 'overall survival of 16.9 months' resulted in a claim which could not be substantiated. A breach of Clause 7.4 was ruled.

The Panel noted that the 'Dear Doctor' letter referred to median overall survival 'immediately following induction' with Alimta/cisplatin. Section 5.1 of the Alimta SPC referred to median overall survival 'Following Alimta plus cisplatin induction' (13.9 months) and median overall survival 'from the start of Alimta plus cisplatin first-line induction' (16.9 months). In the Panel's view, it was likely that some readers would assume that 'immediately following induction' as used in the 'Dear Doctor' letter, was the same as 'Following Alimta plus cisplatin induction' as used in the SPC. This was not so. The Panel considered that the letter was not entirely clear from which time point the 16.9 months survival had been measured. The letter was misleading in that regard and a breach of Clause 7.2 was ruled.

Complaint received **17 April 2013**

Case completed **17 May 2013**

ALMIRALL/DIRECTOR v LEO

Alleged breach of undertaking

Almirall alleged that two Leo Pharma advertisements for Picato (ingenol mebutate) gel, published in March and April 2013 breached the undertaking given by Leo in Case AUTH/2583/3/13.

The case was taken up by the Director as the Authority was responsible for ensuring compliance with undertakings.

Although Leo had changed the advertisements, Almirall alleged that the new advertisements remained misleading and exaggerated. Failing to comply with an undertaking brought discredit upon, or reduced confidence in, the pharmaceutical industry and a breach of Clause 2 was also alleged.

The detailed response from Leo is given below.

The Panel noted 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 Panel noted that the two advertisements identified by Almirall were not new material prepared by Leo subsequent to Case AUTH/2583/4/13. They were part of Leo's campaign for Picato which predated the undertaking given in Case AUTH/2583/4/13 by Leo on 4 April. Leo submitted that the advertisements at issue were caught by that undertaking and they had thus been withdrawn. The copy deadlines for the publications identified by Almirall predated both the notification of the Panel's ruling in Case AUTH/2583/4/13 (25 March) and the undertaking.

Noting the date of the undertaking and copy deadlines for the publications in question the Panel considered that Leo had not failed to comply with its undertaking given in the previous case and ruled no breach of the Code including Clause 2.

Almirall Limited alleged that two advertisements (refs 4340a/00016(1)b and 4340a/0006(1)a) for Picato (ingenol mebutate) gel, breached the undertaking given by Leo Pharma in Case AUTH/2583/3/13. Almirall noted that the advertisements had been published in the BMJ (23/3/13 and 30/3/13), MIMS (April 2013), GP magazine, Dermatological Nursing magazine and Guidelines in Practice.

Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults.

The case was taken up by the Director as the Authority was responsible for ensuring compliance with undertakings.

COMPLAINT

Almirall noted that both advertisements at issue were circulated in the medical press by Leo, subsequent to the Panel's ruling of 25 March 2013 in Case AUTH/2583/3/13.

Almirall noted that although Leo had changed the advertisements found to be in breach, the newly worded advertisements remained misleading and exaggerated, and thus did not reflect the guidance and stipulations given in the Panel's ruling.

Almirall noted that both advertisements featured the headline 'Announcing the arrival of Picato The only 2 or 3 day patient-applied actinic keratosis treatment' despite the Panel's ruling in the previous case that:

> 'The Panel noted that Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults. The headline claim, however, only referred to actinic keratosis without noting the licence restriction. It appeared that Picato could treat any type of actinic keratosis which was not so. In that regard the Panel did not consider that the advertisement encouraged the rational use of the medicine. The provision of the indication in full in the prescribing information did not negate the otherwise misleading impression. A breach of Clause 7.10 was ruled.'

Almirall also noted that in Case AUTH/2583/3/13 the Panel further stated that:

> '.... The claim together with the image of the high speed train might be taken to relate to the speed of effect of Picato. In that regard the Panel noted that the optimum effect of treatment could only be assessed approximately 8 weeks (56 days) after treatment. The Panel considered that the claim was exaggerated as alleged. A breach of Clause 7.10 was ruled.'

Given the above, Almirall alleged that with its new advertisements Leo had failed to comply with its undertaking in breach of Clause 25.

Almirall further alleged that Leo's distribution of such advertisements, even after a clear ruling and guidance from the PMCPA brought discredit upon, or reduced confidence in, the pharmaceutical industry in breach of Clause 2.

RESPONSE

Leo submitted that the complaint related to advertisements that were submitted to journals and/or were in the process of being published before the ruling in Case AUTH/2583/3/13.

Leo provided details of the copy deadlines for each publication which were between 1 and 19 March 2013. The publication dates were mostly in March other than MIMS April. Leo submitted that the copy deadline for each of the publications cited by Almirall fell before the date of the original ruling in Case AUTH/2583/3/13 on the 25 March. Therefore, it would have been impossible to stop the publication of the advertisements in these journals and many were already circulated before the ruling.

Leo noted that Almirall had advertisements in some of the same publications and so should have known the publication/copy dates.

Leo stated that, contrary to Almirall's view, it had taken the recent breach very seriously and, on the day that it was notified of the Panel's ruling, 25 March, it withdrew further print copies of all advertisements, even though there had been no specific complaint against the advertisement that was in use at that time. Leo submitted that it had adhered to its own rigorous internal standards and timelines for the recall (documented through standard operating procedures).

Work then began on a new version of the advertisement and took into account the areas where the company was previously found in breach and also addressing the Panel's concerns on some areas where it was not found in breach.

Leo reiterated, in full support of the PMCPA's ruling, that appropriate measures were taken to withdraw and amend the Picato advertisement.

PANEL RULING

The Panel noted 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 Panel noted that the two advertisements identified by Almirall were not new material prepared by Leo subsequent to Case AUTH/2583/4/13. They were part of Leo's campaign for Picato which predated the undertaking given in Case AUTH/2583/4/13 by Leo on 4 April. Leo submitted that the advertisements at issue were caught by that undertaking and they had thus been withdrawn. The copy deadlines for the publications identified by Almirall predated both the notification of the Panel's ruling in Case AUTH/2583/4/13 (25 March) and the undertaking. It was thus not possible for Leo to prevent their publication.

Noting the date of the undertaking and copy deadlines for the publications in question the Panel considered that Leo had not failed to comply with its undertaking given in the previous case and ruled no breach of Clause 25 and consequently no breach of Clause 2.

Complaint received **23 April 2013**

Case completed **17 May 2013**

CASE AUTH/2598/4/13

CONSULTANT RHEUMATOLOGIST v ROCHE

Promotion of Mabthera

A consultant rheumatologist alleged that a talk about ANCA [anti-neutrophil cytoplasmic antibody]-associated vasculits (AAV), given at a national rheumatology conference, was excessively promotional and against the spirit of the Code. The talk was sponsored by Roche. Roche marketed Mabthera (rituximab) which was recently licensed for the treatment of two forms of AAV, but not for a third.

The complainant noted that the speaker repeatedly stated that he could not refer to rituximab and vasculitis, but that a subsequent speaker in another session would tell them all they needed to know.

The detailed response from Roche is given below.

The Panel noted that Roche had booked a 30 minute workshop at the conference. Guidelines from the organisers stated that the meeting space would be within the exhibition hall and that the session should be educational rather than promotional. The guidelines did not define either term. Examples of acceptable topics included, *inter alia*, educating delegates on a product. The Panel noted that such a presentation would satisfy the broad definition of promotion given in the Code. The Panel queried whether a trade exhibition hall was an appropriate space for a non-promotional presentation.

When Roche engaged the speaker to talk about AAV for rheumatologists it was a therapy area in which the company had no licensed medicine; a relevant licence was obtained for Mabthera the day before the presentation. The Panel noted that the speaker agreement, certified in January 2013, stated that the objective of the session was to increase the awareness of the presentation, diagnosis and management of the three forms of AAV amongst rheumatologists. It also stated that the presentation was to be non-promotional with no proactive mention of Mabthera. Two of the speaker's slides, however, referred to Mabthera and in addition, both parties agreed that the speaker had referred delegates to a subsequent session in the main conference programme where rituximab in AAV would be discussed. In the Panel's view the slides and speaker's comments meant that the presentation, although highly educational, was promotional. The presentation was delivered on the day after a licence was granted allowing the use of Mabthera in two forms of AAV. The speaker's final slide referred to the use of biologics in AAV without qualification and so appeared relevant to all forms of AAV. The Panel thus considered that the presentation implied that Mabthera could be used in all forms of AAV which was not in accordance with the terms of its marketing authorization and a breach of the Code was ruled.

The Panel noted that Roche had certified the speaker's slides whilst the licence for the use of Mabthera in AAV was pending. The Panel assumed that Roche would know that it would not include the third form of AAV. The Panel noted that although the speaker had requested that the final slide be retained, Roche should have ensured that, irrespective of his wishes, it had complied with the Code. Given its ruling above the Panel considered that high standards had not been maintained and a breach of the Code was ruled.

The Panel noted that as the meeting programme clearly stated that the session in question was associated with Roche, attendees would expect to hear about the sponsor's medicines. The session was not portrayed as a non-promotional event. In that regard the Panel did not consider that the promotional nature of the session had been disguised and no breach of the Code was ruled.

A consultant rheumatologist complained about a talk he/she attended at a national annual conference for rhematologists. The talk, sponsored by Roche Products Limited, was entitled 'ANCA [anti-neutrophil cytoplasmic antibody]-associated vasculitis for rheumatologists'. The complainant presumed that the speaker was paid by Roche to give the talk as he was a world expert in the field of vasculitis.

The indications for Mabthera (rituximab) included in combination with methotrexate to treat adult patients with severe active rheumatoid arthritis who had an inadequate response or intolerance to other disease modifying anti-rheumatic drugs (DMARD) including one or more tumour necrosis factor (TNF) inhibitor therapies. The day before the presentation, Mabthera was also licensed for use in combination with glucocorticoids, for the induction of remission in adult patients with severe, active granulomatosis with polyangitis (Wegener's) (GPA) and microscopic polyangitis (MPA). Both conditions were forms of ANCA-associated vasculitis. Mabthera was not licensed for a third form of ANCA-associated vasculitis ie eosinophilic granulomatosis with polyangitis (Churg Strauss Syndrome (CSS)).

COMPLAINT

The complainant stated that the speaker repeatedly stated that he was not allowed to mention rituximab, or the 'R' word in the context of vasculitis, because of the Code. He also stated that he would end the session early and urged everyone to attend the next timetabled session by his colleague which would tell them everything they needed to know about rituximab in vasculitis.

The complainant alleged that this was excessive

promotion of a product which went against the spirit of the Code.

When writing to Roche, the Authority asked it to consider the requirements of Clauses 3.2, 9.1 and 12.1 of the Code.

RESPONSE

Roche explained that the session in question was a new venture by the conference organisers as part of the 2013 meeting and slots were offered to potential sponsors. Roche booked the 11.00-11.30am slot on 23 April 2013, as part of its conference booking made on 5 September 2012. At the time of booking, information on the conference website confirmed that the session would be in a separate, sectioned off area of the exhibition hall. There was no prior knowledge of the detailed main session programme for that day; such detail was only available on the conference website from December 2012. A copy of the exhibition booking form was provided.

Roche confirmed with the organisers the non-promotional and educational expectation of the sessions, which were open to all delegates. Clarification was sought because the content as stated in the conference guidelines (copy provided) allowed for education on a product. The guidelines did not allow for the session to be advertised by the use of company flyers, however promotion of the session was permitted from the company stand and outside the session space at the allocated time.

As the session was non-promotional, Roche considered that it would have been inappropriate to promote the meeting from a promotional stand. Roche staff were thus briefed not to actively encourage attendance at this Roche organised session. A copy of the staff briefing slides was provided.

Roche chose the session topic "ANCA-associated vasculitis (AAV) for rheumatologists" as an area of continued unmet educational need, particularly since the diagnosis of AAV was complex and often missed by non-specialist rheumatologists. Roche was especially mindful of the pending outcome of the Mabthera licence submission for the indication of two forms of AAV. Due to this, even more care was taken to ensure the total non-promotional objectives of the session.

The speaker was engaged by Roche through a consultancy agreement to present on the topic of 'ANCA-associated vasculitis (AAV) for rheumatologists'. The agreement detailed the objective of the session: to increase awareness of the presentation, diagnosis and management of three forms of AAV. The agreement specified the non-promotional requirement for the presentation in four instances, and explicitly stated that no proactive mention of rituximab was to be made. The consultancy agreement was discussed with the speaker in February 2013 to ensure the objectives and non-promotional content of the presentation were clear. The speaker considered that rituximab should be discussed for completeness, however, Roche reiterated that rituximab should not be discussed as part of the presentation. The signed consultancy agreement and accompanying certificate were provided.

The speaker agreed to omit data slides on rituximab. However, he requested that a final summary slide which listed the clinical trials in AAV that had been conducted with a variety of biologics, including rituximab, be retained. The session slides were reviewed and approved by Roche, to confirm consistency with the directions provided in the consultancy agreement, factual accuracy, and that they complied with the Code. The slides and accompanying approval sign-off were provided.

Roche met the speaker immediately before the session started and he confirmed that he understood the non-promotional intent of the presentation and the requirement not to proactively mention rituximab. At the start of the presentation, he stated that he was not allowed to discuss rituximab as part of the presentation. He also stated once that there was a main program session where the rituximab trial data in AAV would be presented. The speaker's presentation did not finish early. A statement from a company employee detailing all interactions with the speaker and what he heard stated at the session was provided.

The main conference programme which followed Roche's session, ran seven parallel sessions. One of these sessions 'Biologics in connective tissue disease' presented three topics, one of which was 'Rituximab in ANCA-associated vasculitis (AAV)'. This topic was selected by the conference organisers.

The speaker considered that to discuss AAV without mentioning rituximab was unbalanced and therefore, he referred to the main conference programme session for those who wanted information on rituximab. A copy of an e-mail from the speaker confirming his opinion and reason for referencing the main session was provided.

In relation to Clause 3.2 Roche submitted that rituximab received a licence for two forms of vasculitis on 22 April 2013, therefore referring to rituximab in an educational session on AAV was not inconsistent with the particulars listed in the summary of product characteristics. As previously detailed, the session was designed to raise awareness of a disease area of high unmet medical education need, and therefore was organised as a non-promotional event, with no intent to promote or solicit any discussions on rituximab. Furthermore, the consultancy agreement confirmed the non-promotional objective of the presentation and the direction not to discuss rituximab. The session slides contained no promotional content. There was no promotion of the session from the stand or by company representatives.

Roche submitted that it had complied with Clause 20.1 as detailed in the signed consultancy agreement. Roche ensured that the content of the

session slides complied with both the consultancy agreement and Clause 3.2. The consultancy agreement explicitly stated that there was to be no proactive mention of rituximab, which was reinforced during the 13 February verbal briefing. Staff were briefed not to encourage attendance at the session. In Roche's view these steps demonstrated that there was no intent to use the session as 'teaser' advertising, as described in the supplementary information to Clauses 9.1 and 9.2. High standards were maintained during the planning and delivery of this session.

Roche submitted that its sponsorship of the session was declared in the conference program in accordance with Clause 9.10. Roche had no prior knowledge of the seven parallel program sessions that would follow the session at issue. The educational intent of the Roche session was detailed in the consultancy agreement, demonstrated in the session slides and was consistent with the non-promotional and educational objective as stipulated in the relevant conference guidelines. The materials and the activity were neither promotional in nature nor disguised in terms of Roche's involvement.

In conclusion Roche submitted that the session was non-promotional in accordance with the conference guidelines. The AAV session topic was a disease for which rituximab had a licensed indication. The speaker's reference to the main conference program session on the same topic, which followed the Roche sponsored session was not made repeatedly, and was done to complete the scientific content of his presentation. Roche concluded that there was no excessive promotion of rituximab at the session.

PANEL RULING

The Panel noted that Roche had booked the 30 minute workshop at the meeting. Guidelines from the organisers stated that the session would be based within the exhibition hall and that the content of the session should be educational rather than promotional. The guidelines did not define either term. Examples of acceptable topics included, *inter alia*, educating delegates on a product. The Panel noted that such a presentation would satisfy the broad definition of promotion given in Clause 1.2. The Panel queried whether a trade exhibition hall was an appropriate space for a non-promotional presentation.

Roche had engaged a speaker to talk about AAV for rheumatologists, a therapy area in which, when the speaker was engaged, Roche had no licensed medicine; a relevant licence was obtained for Mabthera the day before the presentation. The Panel noted that the speaker agreement, certified late January 2013, stated that the objective of the session was to increase the awareness of the presentation, diagnosis and management of GPA, MPA and CSS amongst rheumatologists. It also stated that the presentation was to be non-promotional with no proactive mention of Mabthera. Two of the speaker's slides, however, referred to Mabthera. One of the slides referred to cyclophosphamide plus corticosteroids and then mentioned rituximab in brackets (the Panel did not know the significance of this statement) and the final slide, which the speaker had argued to retain, was headed 'Biologics in ANCA associated vasculitis' and stated that for rituximab, *inter alia*, there had been 3 prospective trials and 4 case series. The following was also stated '2008 – 10 – Rituxvas and RAVE, non-inferiority, as effective in induction as cyclo but no decrease in toxicity'. In addition to the slides the Panel noted that both parties agreed that the speaker had referred delegates to a subsequent session, which was part of the main conference programme, where rituximab trial data in AAV would be discussed. In the Panel's view the slides and speaker's comments about rituximab and its use in AAV was sufficient to mean that the presentation, although highly educational, was promotional under the Code. The presentation was delivered on the day after a licence was granted allowing the use of Mabthera in two forms of AAV ie GPA and MPA. Mabthera was not licensed for use in the third form, CSS. The speaker's final slide referred to the use of biologics in ANCA associated vasculitis without qualification and so appeared relevant to all forms of AAV. The Panel thus considered that the presentation implied that rituximab could be used in all forms of AAV which was not in accordance with the terms of the Mabthera marketing authorization and a breach of Clause 3.2 was ruled.

The Panel noted that the speaker's slides had been certified by Roche on 11 and 12 April when the company had no licence for the use of Mabthera in ANCA associated vasculitis and although a licence application was pending, the Panel assumed that Roche would know that it would not include CSS. The Panel noted that although the speaker had requested that the final slide be retained, Roche should have ensured that, irrespective of the speaker's wishes, it had complied with the Code. Given its ruling above the Panel considered that high standards had not been maintained and a breach of Clause 9.1 was ruled.

The Panel noted that the meeting programme clearly stated that the session in question was associated with Roche. In that regard the Panel considered that delegates attending the session would expect to hear about the sponsor's medicines. The session was not portrayed as a non-promotional event. In that regard the Panel did not consider that the promotional nature of the session had been disguised and no breach of Clause 12.1 was ruled.

Complaint received **29 April 2013**

Case completed **21 June 2013**

ANONYMOUS v MERCK SHARP & DOHME

Cerazette rebate scheme

An anonymous, non-contactable complainant alleged that a retrospective rebate scheme for Cerazette, an oral contraceptive marketed by Merck Sharp & Dohme, was an inducement to prescribe in breach of Clause 2 of the Code.

The complainant noted that several different generic versions of Cerazette had recently become available, resulting in potential loss of market share. To counter this, Merck Sharp & Dohme had offered clinics, hospitals, etc a retrospective rebate.

The detailed response from Merck Sharp & Dohme is given below.

The Panel noted that the complainant was anonymous and uncontactable. 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 noted that the Code excluded from the definition of promotion, measures or trade practices relating to prices, margins or discounts which were in regular use by a significant proportion of the pharmaceutical industry on 1 January 1993. Further, the supplementary information to the Code, Terms of Trade, stated that such measures or trade practices were excluded from the provisions of that clause. The terms prices, margins and discounts were primarily financial terms. The Panel noted that other trade practices were subject to the Code and had to comply with it.

The Panel noted that Merck Sharp & Dohme denied offering retrospective rebates as alleged by the complainant. It did have other discount arrangements in place but these were not retrospective. The Panel noted that it was not possible to contact the complainant for further information. The Panel considered that whilst the subject of complaint was potentially within the scope of the Code, in that there was no material before the Panel to demonstrate that retrospective discounts had been in regular use by a significant proportion of the pharmaceutical industry on 1 January 1993, there was no evidence that the company had undertaken such activity in relation to Cerazette as alleged. The complainant had not discharged his/her burden of proof and the Panel thus ruled no breach of the Code, including no breach of Clause 2.

An anonymous, non-contactable complainant complained about a retrospective rebate scheme for Cerazette, an oral contraceptive, marketed by Merck Sharp & Dohme Limited.

COMPLAINT

The complainant stated that several different generic versions of Cerazette had recently become available, resulting in potential loss of market share. To counter this, Merck Sharp & Dohme had offered clinics, hospitals, etc a retrospective rebate on their use of Cerazette over a 12 month period.

The complainant alleged that a retrospective rebate was an inducement to prescribe and therefore a *prima facie* breach of Clause 2 of the Code.

When writing to Merck Sharp & Dohme, the Authority asked it to consider the requirements of Clause 18.1 of the Code in addition to Clause 2 cited by the complainant.

RESPONSE

Merck Sharp & Dohme was not clear as to what the complainant referred in relation to the statement that it had offered clinics, hospitals etc a retrospective rebate on their use of Cerazette over a 12 month period. Merck Sharp & Dohme did not have any retrospective rebate schemes in place with clinics, hospitals or any other third party. Merck Sharp & Dohme stated that it did not believe that the Cerazette discount arrangements it had in place were relevant. Firstly, it had contracts in place to supply NHS hospitals in England, Scotland and Northern Ireland with Cerazette at a discount. These discounts had been agreed with the respective national purchasing authorities within formal tendering/ contracting procedures and not directly with specific hospitals, hospital departments or clinicians. Under this scheme, hospitals purchased the product at the agreed contract price and, as such, the discount was not retrospective. Secondly, Cerazette was provided to some family planning clinics at a discounted price but, again, the discount was agreed prior to product purchase and not retrospectively.

Merck Sharp & Dohme stated that the discounts on Cerazette did not appear to fit the description of the activity alleged in the complainant's letter. Merck Sharp & Dohme had always understood that discounts fell outside the scope of the Code (Clause 1.2) as they had been in regular use prior to 1993. As such, Merck Sharp & Dohme did not believe this matter should proceed to the Panel.

Merck Sharp & Dohme stated that if the matter did proceed, the Cerazette discounts had been agreed with the purchasing authorities, in the case of the hospital contracts, and with the appropriate decision makers in the case of family planning clinics. Merck Sharp & Dohme stated that no health

professional or administrative staff member had obtained any personal benefit as a result of its discount arrangements. Merck Sharp & Dohme did not consider that this activity constituted a breach of Clause 18.1, or by implication, a breach of Clause 2 which was reserved for particularly serious breaches of the Code.

Merck Sharp & Dohme stated that in common with other companies, it evaluated potential arrangements or schemes including discounts in a number of therapy areas, including contraception. If any of these were to be implemented in due course, they would be subjected to appropriate review and approval from both a legal and a Code perspective.

PANEL RULING

The Panel noted that the complainant was anonymous and uncontactable. 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 noted that Clause 1.2 excluded from the definition of promotion, measures or trade practices relating to prices, margins or discounts which were in regular use by a significant proportion of the pharmaceutical industry on 1 January 1993. Further, the supplementary information to Clause 18.1, Terms of Trade, stated that such measures or trade practices were excluded from the provisions of that clause. The terms prices, margins and discounts were primarily financial terms. The Panel noted that other trade practices were subject to the Code and had to comply with it.

The Panel noted Merck Sharp & Dohme's submission that this case should not proceed to the Panel as, in its view, the practice of discounting fell outside the scope of the Code. Merck Sharp & Dohme referred to Clause 1.2 of the Code. The Panel noted that Clause 1.2 exempted certain trade practices from the definition of promotion as set out above. The Panel noted that the Constitution and Procedure did not permit the case preparation manger to decide whether such a matter was outside the scope of the Code; that was a matter for the Panel.

The Panel noted that Merck Sharp & Dohme denied offering retrospective rebates as alleged by the complainant. It did have other discount arrangements in place but these were not retrospective. The Panel noted that it was not possible to contact the complainant for further information. The Panel considered that whilst the subject of complaint was potentially within the scope of the Code, in that there was no material before the Panel to demonstrate that retrospective discounts had been in regular use by a significant proportion of the pharmaceutical industry on 1 January 1993, there was no evidence that the company had undertaken such activity in relation to Cerazette as alleged. The complainant had not discharged his/her burden of proof and the Panel thus ruled no breach of Clauses 18.1 and 2.

Complaint received **30 April 2013**

Case completed **30 May 2013**

CASE AUTH/2601/5/13

EX-EMPLOYEE/DIRECTOR v GEDEON RICHTER

Breach of undertaking

An ex-employee alleged that a meeting invitation, which was available (22 May) on an events company's website, breached the undertaking given by Gedeon Richter (15 April) in Case AUTH/2580/2/13. When the complaint was submitted the complainant's appeal in Case AUTH/2580/2/13 had yet to be heard.

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

The detailed response from Gedeon Richter is given below.

The Panel noted that a form of undertaking and assurance was an important document. Companies had to give an undertaking that the material in question and any similar material, if not already discontinued or no longer in use, would cease forthwith and give an assurance that all possible steps would be taken to avoid similar breaches of the Code in future. It was very important for the reputation of the industry that companies complied with undertakings.

The Panel noted that Gedeon Richter had accepted the ruling of a breach of the Code in Case AUTH/2580/2/13; the company's undertaking was signed on 15 April and it was stated that 6 March was the last date the material was used or appeared. Although the complainant had appealed the Panel's rulings of no breach in that case, the Panel did not understand why Gedeon Richter believed that its undertaking would not be in force until the final ruling was made. There was nothing in any of the correspondence from the PMCPA to give that impression. The guidelines on company procedures relating to the Code referred to material in breach of the Code being 'quickly and entirely withdrawn from use'.

The Panel considered that as the invitation at issue, which was available on the event company's website after Gedeon Richter had given its undertaking, did not include prescribing information, Gedeon Richter had failed to comply with its undertaking given in the previous case. The Panel ruled a breach of the Code. High standards had not been maintained and a further breach of the Code was ruled.

The Panel noted the importance of complying with undertakings and considered that Gedeon Richter's failure to enforce its undertaking brought discredit upon and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

An ex-employee of Preglem UK (a wholly owned subsidiary of Gedeon Richter) alleged that the company had failed to comply with the undertaking given in Case AUTH/2580/2/13 in relation to a meeting invitation and a breach of Clause 4.1. When the present complaint (Case AUTH/2601/5/13) was submitted certain other rulings in Case AUTH/2580/2/13 were the subject of an appeal from the complainant which had not yet been heard by the Code of Practice Appeal Board.

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 referred to the Panel's ruling of a breach of Clause 4.1 in Case AUTH/2580/2/13 and Gedeon Richter's undertaking which the complainant understood was effective from 15 April 2013.

In Case AUTH/2580/2/13 the Panel had noted that the front page of a meeting invitation featured the brand imagery associated with Esmya (ulipristal acetate). In this regard the Panel considered that the recipients would immediately associate the meeting with Esmya. That invitation was considered promotional and prescribing information should have been included.

In the present case the complainant referred to a very similar invitation currently available (22 May) on the website of Gedeon Richter's events company. A link to the website and a copy of the invitation was provided.

The complainant stated that the invitation (ref GRADV 13/0034) now at issue featured brand imagery which was the same as that at issue in Case AUTH/2580/2/13 and the meeting was similar but the invitation did not contain prescribing information. The brand imagery would be associated with Esmya and the meeting should be expected to be promotional. The complainant alleged a breach of undertaking.

When writing to Gedeon Richter, the Authority asked it to respond in relation to Clauses 25, 9.1 and 2.

RESPONSE

Gedeon Richter noted that the allegation related to an invitation to a meeting which was to take place on 14 May, which could be found on the events company's website. The complainant alleged that as the invitation did not contain the prescribing

information for Esmya the company had breached its undertaking.

Following the Panel's ruling in Case AUTH/2580/2/13, Gedeon Richter informed the Panel that it was satisfied with the Panel's conclusion and submitted its notice of undertaking based on this conclusion. However, the complainant appealed the Panel's ruling. Gedeon Richter thus believed that the case was still open and that its undertaking would not be in force until the final ruling was reached. It was still its firm intent to adhere to the spirit and word of the undertaking in relation to Case AUTH/2580/2/13 and it had begun to take steps to ensure that the prescribing information was on all promotional material that it produced, including meeting invitations. It had contacted the events company to ensure that the prescribing information was included on Gedeon Richter meeting invitations but unfortunately this had not been done when the complainant reviewed the website.

Gedeon Richter was undertaking a comprehensive update of its promotional practices including the introduction of standard operating procedures (SOPs) relating to matters such as meetings and events, medical and educational goods and services, consultancy agreements and many others. The company had also introduced an electronic review and approval tool to allow it to better control its processes and as it believed that the undertaking had not yet come into force it intended to update all materials, including those on the events company's website, in line with its new SOPs and review tool. The company never intended to breach its undertaking and it believed that it would be unfair for it to be found in breach of the Code due to a potential lack of clarity in the process.

In order to avoid any further concern or confusion the company had requested that all of its material be removed from the events company's website until it had received the full and final ruling in Case AUTH/2580/2/13 from the Appeal Board. In the meantime it would be grateful for guidance from the Panel as to the timing of its undertaking and when it could be considered to be in force, particularly as the case to which it related had yet to be concluded.

In summary Gedeon Richter did not believe it had breached Clauses 25, 9.1 or 2 of the Code.

PANEL RULING

The Panel noted that a form of undertaking and assurance was an important document. Companies had to give an undertaking that the material in question and any similar material, if not already discontinued or no longer in use would cease forthwith and give an assurance that all possible steps would be taken to avoid similar breaches of the Code in future. (Paragraph 7.1 of the Constitution and Procedure refers.) It was very important for the reputation of the industry that companies complied with undertakings.

The Panel noted that Gedeon Richter had accepted the ruling of a breach of Clause 4.1 in Case AUTH/2580/2/13; the company's undertaking was signed on 15 April 2013 and it was stated that 6 March was the last date the material was used or appeared. The fact that the complainant had appealed the Panel's rulings of no breach was irrelevant to the status of the undertaking. It was clear from the form that once a company accepted a breach of the Code material had to be withdrawn forthwith; there was no reference to such action being subject to the outcome of a possible appeal of other rulings by the complainant. If a complainant appeal were successful then a respondent company would have to give a further undertaking in relation to the Appeal Board's ruling of a breach.

The letter informing Gedeon Richter that the complainant had appealed did not refer to the undertaking, other than it had been received. The Panel did not understand why Gedeon Richter believed that its undertaking would not be in force until the final ruling was made. There was nothing in any of the correspondence from the PMCPA to give that impression. The guidelines on company procedures relating to the Code referred to material in breach of the Code being 'quickly and entirely withdrawn from use'. The Panel did not accept that there was a lack of clarity in the process. A company could always contact the PMCPA if it was unsure as to what action was required.

The Panel considered that as the invitation for the meeting of 14 May, which was available on the events company's website after Gedeon Richter had given its undertaking, did not include prescribing information, Gedeon Richter had failed to comply with its undertaking given in the previous case. Thus the Panel ruled a breach of Clause 25. High standards had not been maintained and a breach of Clause 9.1 was also ruled.

The Panel noted the importance of complying with undertakings and considered that Gedeon Richter's failure to enforce its undertaking brought discredit upon and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

Complaint received **2 May 2013**

Case completed **6 June 2013**

ANONYMOUS v CHUGAI

Provision of hospitality

An anonymous, non-contactable complainant complained about hospitality provided to health professionals by Chugai Pharma UK.

The complainant stated that at a recent British Society of Haematology meeting he/she was confused by the mixed messages given out by various pharmaceutical companies attending regarding hospitality.

The complainant stated that the local Chugai representative refused to take the complainant's team out for dinner stating 'I am sorry, we are no longer able to do that due to changes in the Code and our company's interpretation of the compliance issues'. The representative also set out the company's policy on this point.

However, the complainant was confused and surprised when he/she witnessed on many occasions another named pharmaceutical company actively entertaining customers and buying them drinks openly in the bar of a named hotel. This was further highlighted when, following the gala dinner, the complainant and many colleagues went back to a named hotel only to be joined by a number of Chugai personnel, one of whom openly bought rounds of drinks for everyone in the bar and proceeded to be loud in his communication with some customers who were obviously his friends! The complainant thought this happened at around 2am.

The complainant considered that either he/she had been lied to by the local Chugai representative or had their colleague not read the same documents? The complainant submitted that if the ABPI had laid down ground rules to be followed, then everyone should follow them to the letter of the law.

The detailed response from Chugai is given below.

The Panel noted that the complainant was anonymous and non-contactable. As stated in the introduction to the Constitution and Procedure such complaints were accepted and like all complaints, judged on the evidence provided by the parties. Complainants had the burden of proving their complaint on the balance of probabilities. The Panel noted that as the complainant was anonymous and non contactable it was not possible to ask the complainant for further information.

The Panel noted that in addition to detailed requirements in the Code companies were required to have a written document setting out their policies on meetings and hospitality and the associated allowable expenditure.

The Panel noted that the parties' accounts of activities in the bar differed. The complainant had stated that on the night of the gala dinner he/she and his/her colleagues were joined at the bar by a number of Chugai personnel one of whom purchased rounds of drinks for everyone in the bar and spoke loudly. Chugai submitted that on the night in question whilst its employees acknowledged health professionals whom they knew on entering the bar they sat separately in a booth and drinks were purchased for company personnel only. The company receipts were consistent with the company's submission in terms of the number of drinks purchased. The Panel had no way of checking who had consumed these drinks. The company submitted that none of its employees had behaved in an unruly or loud manner.

The Panel noted that the complainant bore the burden of proof and further noted from the introduction to the Constitution and Procedure that complaints were decided on the evidence provided by the parties. The Panel considered that bearing in mind all the evidence before it the complainant had not established that Chugai had provided inappropriate hospitality as alleged. No breaches of the Code were ruled.

An anonymous, non-contactable complainant complained about hospitality provided to health professionals by Chugai Pharma UK Limited. The complainant also named another pharmaceutical company and so the matter was also taken up with that company (Case AUTH/2603/5/13).

COMPLAINT

The complainant stated that he/she wrote with some disillusionment following his/her attendance at the recent British Society of Haematology meeting. Historically this meeting had not only been a great source of learning but also a very hospitable time with gratitude to various pharmaceutical companies. However, at this year's meeting the complainant was confused by the mixed messages given out by various pharmaceutical companies attending, especially as he/she had been informed many times over the past 12 months that taking health professionals out for meals and buying them alcoholic drinks was now not acceptable.

The complainant stated that the reason for his/her missive, was that his/her local Chugai representative, when asked if he/she could take the complainant's team out for dinner replied 'I am sorry, we are no longer able to do that due to changes in the Code and our company's interpretation of the compliance issues'. The representative went on to state 'We are

now meant to go out to dinner as part of a company group with no customers present; if they are in the same building or in fact join us, a decision has to be taken as to whether we stay or leave; the same applies to having drinks in pub/club or hotel bar' (sic).

The complainant did not fully agree with this but could see that all companies were now obviously making a stance in this area much to his/her dismay.

However, the complainant was confused and surprised when he/she witnessed on many occasions another named pharmaceutical company actively entertaining customers and buying them drinks openly in the bar of a named hotel. This was further highlighted when, following the gala dinner, the complainant and many colleagues went back to the hotel only to be joined by a number of Chugai personnel, one of whom openly bought rounds of drinks for everyone in the bar and proceeded to be loud in his communication with some customers who were obviously his friends! The complainant thought this happened at around 2am.

The complainant considered that either he/she had been lied to by the local Chugai representative or had their colleague not read the same documents? The complainant submitted that if the ABPI had laid down ground rules to be followed, then everyone should follow them to the letter of the law.

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

RESPONSE

Chugai noted that the complaint was from an anonymous, non-contactable complainant who had not submitted any evidence or material to support his/her complaint.

Chugai took the allegations extremely seriously. All staff were aware of the need to maintain high standards between themselves and health professionals in line with the Code.

The director of finance and human resources and compliance officer had both interviewed all employees individually that attended the event. They had also reviewed the bar bills that were charged to the rooms of all the attendant employees. Chugai believed that it had acted properly and was confident that it had not breached the Code.

Chugai explained that the British Society of Haematology was an established learned medical society with an established annual conference. The 53rd annual event took place between 15 -17 April 2013 in Liverpool. Chugai was a sponsor at the event and a number of its employees had attended.

Chugai explained that it was strict company policy that employees did not purchase meals or drinks for health professionals outside of its company guidelines. It was therefore not surprising that the complainant articulated the fact that a representative had explained this policy to him/her.

Ten Chugai staff were at the named hotel for the duration of the conference. The gala dinner was held on the evening of 16 April, but no Chugai employee attended. Instead the Chugai employees went to a local restaurant. No health professionals were present for this event. Seven employees returned to the hotel bar at approximately 00.45.

On entering the bar, it was clear that some health professionals were also present. Chugai understood that those health professionals had returned from the gala dinner at approximately 00.15. The Chugai employees understandably acknowledged the health professionals in the bar area on their immediate arrival, however in line with company policy the Chugai group sat separately to everyone else. No drinks were ordered until the Chugai employees were seated. All employees had since reaffirmed their awareness of company policy, which was to sit separately where possible, to not engage directly with any health professional and under no circumstances purchase any subsistence or beverage for a health professional in a social setting.

Chugai explained that the bar area was L-shaped and open plan with a number of horseshoe-shaped pod booths. This gave the Chugai staff a distinct sense of separateness to the rest of the bar area. No health professional visited the Chugai employees at the booth or sat with them. No drinks were purchased for anyone other than Chugai staff.

Receipts from the evening showed that a round of 7 drinks was purchased at 01.10 (1 Baileys, 1 wine and 5 beers) with a further glass of wine at 01.13. A double round of drinks was then purchased at 01.43, just before the bar closed (3 Baileys, 8 beers, 2 waters and 1 orange juice). The employees stated that none of these drinks were purchased for or consumed by any health professional. Copies of the receipts were provided.

Chugai employees who were present during this time stated that at no point did any employee behave in an unruly or loud manner.

Chugai provided a copy of its policy on meetings and hospitality and noted that all of the attendant employees were last trained on it in November/ December 2012. Chugai also provided a list of the names and titles of the employees present, and copies of the ABPI examination certificates for the representatives.

Chugai stated that it had taken this anonymous complaint extremely seriously and had performed a thorough investigation; the company strenuously denied any breach of the Code. There was no evidence that any member of staff purchased drinks for health professionals and as such Chugai refuted any breach of Clause 19.1.

Chugai submitted that there was no evidence that any of its staff had acted in an inappropriate

manner. The Appeal Board had confirmed in Case AUTH/2509/6/12 that it was not inappropriate *per se* for an employee to be in the same social setting as health professionals provided that the employee did not breach the Code. Chugai refuted any breach of Clause 9.1.

Chugai was pleased to find that the request by the anonymous complainant to entertain his/her team for dinner was refuted in line with its guidelines.

Finally Chugai was very concerned that the complainant was anonymous and uncontactable. The complainant had failed to supply any evidence or material in support of his/her serious allegations. Chugai was very concerned that this allegation could damage its good reputation.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. As stated in the introduction to the Constitution and Procedure such complaints were accepted and like all complaints, judged on the evidence provided by the parties. Complainants had the burden of proving their complaint on the balance of probabilities. The Panel noted that as the complainant was anonymous and non contactable it was not possible to ask the complainant for further information.

Clause 19.1 stated that hospitality must be strictly limited to the main purpose of the event and must be secondary to the purpose of the meeting ie subsistence only. The level of subsistence offered must be appropriate and not out of proportion to the occasion. The supplementary information to Clause 19.1 made it clear that the provision of hospitality was limited to refreshments/subsistence (meals and drinks), accommodation, genuine registration fees and the payment of reasonable travel costs which a company might provide to sponsor a delegate to attend a meeting. In determining whether a meeting was acceptable or not consideration needed to be given to the educational programme, overall cost, facilities offered by the venue, nature of the audience, subsistence provided and the like. It should be the programme that attracted delegates and not the associated hospitality or venue. The supplementary information also stated that a useful criterion in determining whether the arrangements for any meeting were acceptable was to apply the question 'would you and your company be willing to have these arrangements generally known?' The impression that was created by the arrangements for any meeting must always be kept in mind.

The Panel noted that in addition to detailed requirements in the Code regarding meetings and the provision of hospitality companies were required to have a written document setting out their policies on meetings and hospitality and the associated allowable expenditure. The Panel noted that company policies and procedures had to be in line with the Code. A company's policies might be even more restrictive than the Code. It may be that this had contributed to the complainant's concerns.

The Panel considered that the company's submission that the 'Appeal Board had confirmed in Case AUTH/2509/6/12 that it was not inappropriate *per se* for an employee to be in the same social setting as health professionals provided that the employee did not breach the Code' was not a fair reflection of the Appeal Board's consideration in that case. In Case AUTH/2509/6/12 the Appeal Board considered that whether such activity was acceptable would depend upon the circumstances of each individual case.

The Panel noted that the complainant had commented on the refusal of a Chugai representative to take the complainant and his/her team out to dinner. Whilst this refusal had triggered the complaint the Panel did not consider that it was the subject of complaint.

The Panel noted Section 5.1.2, Hospitality, of the company standard operating procedure (SOP) (MP 006.02) stated it was acceptable to provide low key subsistence if the health professional had received sponsorship of full registration, travel and accommodation costs. Low key subsistence could also be provided if a non third party meeting had been organised (advisory board meeting or a satellite meeting). The SOP stated that it was not possible to provide subsistence to health professionals who had received part or no funding at all. It was also unacceptable to make impromptu arrangements on the day of the meeting as this would be deemed social entertainment. In addition Chugai had submitted that it was a strict company policy that employees did not purchase meals or drinks for health professionals outside its internal guidelines.

The Panel noted that the parties' accounts of activities in the bar differed. The complainant had stated that on the night of the gala dinner he/she and his/her colleagues were joined at the bar by a number of Chugai personnel one of whom purchased rounds of drinks for everyone in the bar and spoke loudly. Chugai submitted that on the night in question whilst its employees acknowledged health professionals whom they knew on entering the bar they sat separately in a booth and drinks were purchased for company personnel only. The company receipts were consistent with the company's submission in terms of the number of drinks purchased. The Panel had no way of checking who had consumed these drinks. The company submitted that none of its employees had behaved in an unruly or loud manner.

The Panel considered that there was no evidence before it to support the complainant's allegations. The complainant had not discharged his/her burden of proof and the Panel thus ruled no breach of Clauses 9.1 and 19.1.

The Panel noted that the complainant bore the burden of proof and further noted from the introduction to the Constitution and Procedure that complaints were decided on the evidence provided by the parties. The Panel considered that bearing in mind all the evidence before it the complainant

had not established that Chugai had provided inappropriate hospitality as alleged. No breach of Clauses 9.1 and 19.1 were ruled.

Complaint received **7 May 2013**

Case completed **17 June 2013**

CASE AUTH/2603/5/13

ANONYMOUS v ROCHE

Provision of hospitality

An anonymous, non-contactable complainant complained about hospitality provided to health professionals by Roche Products.

The complainant stated that at a recent British Society of Haematology (BSH) meeting he/she was confused by the mixed messages about hospitality given out by the various pharmaceutical companies attending regarding hospitality.

The complainant noted that a representative from a named pharmaceutical company refused to take the complainant's team out for dinner stating this was due to changes in the Code and the company's interpretation of the compliance issues. The representative set out the company's policy on this point.

However, the complainant was confused and surprised when he/she witnessed on many occasions Roche actively entertaining customers and buying them drinks openly in the bar of a named hotel. This was further highlighted when, following the gala dinner, the complainant and many colleagues went back to the named hotel only to be joined by a number of personnel from the other pharmaceutical company, one of whom openly bought rounds of drinks for everyone and was loud in his communication with some customers who were obviously his friends! The complainant thought this happened at around 2am.

The complainant considered that either he/she had been lied to by the local representative from the other pharmaceutical company or had their colleague not read the same documents? The complainant submitted that if the ABPI had rules to be followed, then everyone should follow them to the letter.

The detailed response from Roche is given below.

The Panel noted that as stated in the introduction to the Constitution and Procedure, anonymous complaints were accepted and like all complaints, judged on the evidence provided by the parties. Complainants had the burden of proving their complaint on the balance of probabilities. The Panel noted that as the complainant was also non-contactable it was not possible to ask him/her for further information.

The Panel noted that in addition to detailed requirements in the Code companies were required to have a written document setting out their policies on meetings and hospitality and associated allowable expenditure.

The Panel noted that Roche had provided a detailed account of subsistence provided during the conference including that provided at venues other than the hotel bar. The Panel limited its consideration to the subject of the complaint; subsistence provided in the hotel bar.

The Panel noted that the conference lasted from Monday, 15 April to Wednesday, 17 April. On Sunday, 14 April Roche held a meeting in the hotel bar to review logistics for the week. Four health professionals attended one of whom, an active member of BSH, had asked Roche for advice about optimizing future BSH conferences from a company perspective; Roche had not sponsored his/her attendance at the meeting and he/she was not providing a service for Roche. This health professional also accompanied five Roche employees to dinner that evening. Roche submitted that all attendees returned to the hotel rooms without going to the hotel bar. The Panel noted that in relation to subsistence at the hotel bar, 13 drinks had been provided for 10 individuals over 2 hours and considered that the level of hospitality was not unreasonable in relation to three of the four health professionals involved. The Panel noted that whilst the complaint concerned subsistence provided at the hotel bar, to consider whether this was reasonable in relation to the health professional who subsequently accompanied Roche staff to the restaurant, it had to bear in mind the overall level of subsistence provided that evening. In that regard the Panel noted that according to Roche, five employees and one agency member of staff accompanied the health professional concerned to the restaurant. The bill provided by Roche however indicated that there were five people present not seven as submitted by Roche. The bill stated that a 10% service charge would only be added to groups of 6 or more. 10% service charge had been added to the bill. The position was unclear. The bill totalled £243.27 including £82.80 spent on wine.

The Panel was concerned about the subsistence provided to the health professional on Sunday, 14 April. The Panel noted that the educational content of the conference began on Monday; there was thus no educational programme on the Sunday and Roche had not argued that the subsistence was secondary to a conference educational event. The Panel noted that pre-dinner drinks at the hotel bar and a meal at a local restaurant had been provided for what should have been a relatively straightforward discussion. The Panel was concerned about the informal nature of the arrangements including the absence of an agenda bearing in mind the overall level of subsistence provided which included a restaurant meal. The company should be able to clearly demonstrate that the subsistence was secondary to the discussion in question. The Panel noted that the complainant bore the burden of proof and further noted, from the introduction to the Constitution and Procedure, that complaints were decided on the evidence provided

by the parties. The Panel considered that, given all the evidence before it and for the reasons set out above, the subsistence provided to the health professional in question at the hotel bar, noting the overall level of subsistence provided to him/her that evening, was, on balance, contrary to the requirements of the Code and a breach was ruled.

The Panel noted that Roche staff went to the hotel bar on the Monday evening but were not accompanied by health professionals nor according to Roche were health professionals otherwise present at the bar. On Tuesday, 16 April Roche provided early evening drinks at the hotel bar to, *inter alia*, two health professionals who were speakers for Roche at the conference; £74.40 was spent on 16 drinks for nine people. After dinner at a local restaurant three Roche staff and one health professional returned to the bar and shared a bottle of wine. A group of health professionals who came into the bar shortly afterwards were told that Roche could not purchase a drink for them as they were leaving the bar shortly. The Roche staff did not consume the wine that was then brought for them by one of these health professionals. The Panel noted that whilst the complaint concerned subsistence provided at the hotel bar, to consider whether this was reasonable it had to bear in mind the overall level of subsistence provided to the individual health professional who was accompanied by Roche employees throughout the evening. In this regard the Panel noted the restaurant bill for four individuals came to £179.90 including £53.36 for drinks. The Panel considered that bearing in mind the overall level of subsistence provided to this individual throughout the evening, the level of subsistence provided at the bar was not unreasonable.

The Panel noted that it had raised some concerns as set out above and had ruled one matter in breach of the Code. In relation to the subsistence provided to health professionals (other than the one health professional on Sunday, 14 April), the Panel ruled no breach of the Code.

An anonymous, non-contactable complainant complained about hospitality provided to health professionals by Roche Products Limited. The complainant also named another pharmaceutical company and so the matter was additionally taken up with that company (Case AUTH/2602/5/13). Roche also decided to make a voluntary admission as a result of its investigation into this case, Case AUTH/2609/6/13.

COMPLAINT

The complainant stated that he/she was disillusioned following his/her attendance at the recent British Society of Haematology (BSH) meeting which historically had not only been a great source of learning but also a very hospitable time with gratitude to various pharmaceutical companies. However, at this year's meeting the complainant was confused by the mixed messages given out by various pharmaceutical companies attending, especially as he/she had been informed many times over the past 12 months that taking health professionals out for meals and buying them alcoholic drinks was now not acceptable.

The complainant stated that the reason for his/her missive, was that his/her local representative from a named pharmaceutical company, when asked if he/she could take the complainant's team out for dinner replied 'I am sorry, we are no longer able to do that due to changes in the Code and our company's interpretation of the compliance issues'. The representative went on to state 'We are now meant to go out to dinner as part of a company group with no customers present; if they are in the same building or in fact join us, a decision has to be taken as to whether we stay or leave; the same applies to having drinks in pub/club or hotel bar' (sic).

The complainant did not fully agree with this but could see that all companies were now obviously making a stance in this area much to his/her dismay.

However, the complainant was confused and surprised when he/she witnessed on many occasions Roche actively entertained customers and buying them drinks openly in the bar of a named hotel. This was further highlighted when, following the gala dinner, the complainant and many colleagues went back to the named hotel only to be joined by a number of personnel from the other pharmaceutical company, one of whom openly bought rounds of drinks for everyone in the bar and proceeded to be loud in his communication with some customers who were obviously his friends! The complainant thought this happened at around 2am.

The complainant considered that either he/she had been lied to by the local pharmaceutical representative or had their colleague not read the same documents? The complainant submitted that if the ABPI had laid down ground rules to be followed, then everyone should follow them to the letter.

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

RESPONSE

Roche provided copies of its standard operating procedure (SOP) on meetings and hospitality together with the appendices which related to subsistence levels and expenses associated with meetings. Roche noted that the latter stated, *inter alia*, that:

> 'When the meeting involves an overnight stay, post dinner drinks (beer, wine or soft drinks) in the hotel bar area can be offered to delegates, but this is not obligatory. The most senior member of the Roche team will determine the appropriate level of post dinner drinks offered.'

The British Society of Haematology Annual Meeting took place in Liverpool between Monday, 15 April and Wednesday, 17 April 2013. Roche paid for exhibition space at the congress and also held a symposium on Tuesday, 16 April.

The Roche delegation comprised of 26 people; 16 employees (including 4 representatives), 6 agency staff and 4 health professionals. The health professionals were all engaged as speakers at the Roche symposium and Roche funded their meeting registration, travel, accommodation and subsistence. Four staff were responsible for subsistence and the payment where health professionals were in attendance; two brand managers, a medical manager and an oncology relations manager. Roche provided the relevant ABPI Representatives Examination certificates but one employee who paid for a meal at a local restaurant on the evening of Sunday, 14 April, had not taken the ABPI Representatives Examination despite being in a promotional role for over 2 years. (This matter became the subject of a voluntary admission (Case AUTH/2609/6/13)).

Roche detailed the evening activities of its employees for each night of the congress. Unless otherwise stated, the venues for these activities were open to the public and all subsistence provided to health professionals was paid for by a brand manager. In all cases but one the most senior Roche employee present paid for subsistence. All receipts were provided.

Sunday, 14 April
Four Roche employees met at 6pm in the hotel bar and were joined by four health professionals one of whom was a speaker at the Roche symposium. The purpose of the discussion was to review the logistics for events which took place that week at the congress (presentation rehearsal for the Roche symposium and it was anticipated that two of the other health professionals would be involved in filming at a meeting during the congress – see details below). Two further Roche employees also sat near the table but were not part of this discussion. Over the course of 2 hours, thirteen drinks were purchased by two Roche employees for these 10 individuals (10 bottles of beer, 1 pint of beer, 1 orange juice and 1 glass of wine).

Three of the four health professionals left the bar at varying times from 6.30pm and the remaining health professional (who was not one of Roche's speakers nor involved in the filming referred to below, but was a delegate at the congress) joined five Roche employees and one agency member of staff for dinner at a local restaurant. This meal was paid for by a member of staff who was not the most senior member of staff present as two brand managers were also present, however one of these brand managers determined that the level of subsistence was appropriate. This meal finished at approximately 11.30pm and all attendees returned to their respective hotel rooms without going to the hotel bar.

Monday, 15 April
A presentation rehearsal was pre-arranged in the evening for the Roche-sponsored symposium. Two of the health professionals involved in the symposium, four Roche employees and three agency staff attended this meeting which took place in a private room at the hotel. No alcoholic drinks were purchased as part of this meeting.

At 7.30pm ten Roche employees went to a local restaurant for dinner. At approximately 8.40pm a group from a pre-arranged rehearsal meeting, three Roche employees and the two health professionals, went to a pre-arranged dinner at another nearby restaurant. The latter group was joined by a further health professional who had asked to join the group in order to meet one of the other health professionals present with whom he was collaborating on a Roche-supported investigator-sponsored trial. This further health professional was not supported by Roche to attend the congress but was a registered delegate. The booking at the restaurant was originally for seven, however one Roche employee remained at the hotel to amend slides for the symposium and so only six people (three Roche employees and three health professionals) attended the meal. The table was in a private area of the restaurant where no members of the public could overhear any conversation.

After the meal the presentation rehearsal group returned to the meeting room at 10.45pm to meet the agency and another Roche employee to ensure all was in place for the symposium the following day. No health professionals attended this meeting. The group worked together until 12.30am, did not consume any alcohol and then all departed to their own rooms.

At 10.15pm the Roche-only group returned to the hotel and five of the group went to the hotel bar. They had one drink each. No health professionals were in the hotel bar at that time. This group retired to their rooms at 11.30pm.

Tuesday, 16 April
This was the evening of the gala dinner. No Roche employee attended this dinner.

In the afternoon two Roche employees attended a pre-arranged meeting in a hotel meeting room with a health professional engaged as a consultant. This health professional was one of the speakers at the Roche symposium for whom Roche had provided support to attend the congress. The meeting involved filming the consultant speaking and a cameraman was also in attendance. At 5.30pm two Roche employees met the health professional speaker in the hotel bar after concluding some filming and they were joined by the cameraman. Two bottles of beer and two glasses of wine were purchased. They were then joined at approximately 6pm by another Roche employee and another health professional (who was also supported by Roche to attend the meeting as he was a speaker at the Roche symposium). One of the health professionals left the bar at approximately 6.15pm. Three other Roche employees entered the hotel bar at approximately 6.30pm but did not join the original group as meeting discussions were ongoing. Drinks for this group were ordered and placed on the same bill, which was signed for all drinks and closed the order at approximately 7.45pm. Roche noted that although this receipt stated there were four people present, this represented the number of people when the bar order was opened. The number of people for whom drinks were bought was nine.

At 8pm three Roche employees and the remaining health professional then went to a restaurant. There were no other health professionals in the restaurant. The other Roche employees went to another restaurant as a Roche-only group for dinner.

The group of three Roche employees and one health professional arrived back at the hotel at 11.20pm. They went to the bar and at 11.36pm a Roche medical manager ordered a bottle of wine. There were no other health professionals or members of the public in the bar. Shortly afterwards a group of health professionals came into the bar and the Roche employees told them that they could not buy them a drink as they intended to leave the bar shortly. One health professional then insisted on buying glasses of wine for the three Roche employees, however these were left on the bar and not consumed. The three Roche employees discussed that they needed to leave the bar and proceeded to do so. The other Roche group arrived in the hotel bar at approximately 11:45pm and they were informed by the other Roche employees that they should go to their rooms, which they did.

In summary, Roche submitted that whilst it did provided hospitality to certain health professionals during the course of the BSH meeting, this was appropriate, proportionate to the event and secondary to the main purpose of the meeting. It was not, as alleged by the complainant, in the early hours of the morning. Roche thus refuted the allegation of a breach of Clause 19.1. Consequently Roche did not consider that it had failed to maintain high standards whilst attending this meeting and therefore considered that there had been no breach of Clause 9.1.

In response to a request for further information Roche provided a copy of the conference programme for the meeting and the agenda for the Roche symposium that took place during the meeting.

With regard to the fourth health professional to whom subsistence was provided by Roche on the evening of 14 April, Roche explained that he was a consultant haematologist and a delegate at the BSH conference. He was also an active BSH member and in his roles as the latter he had asked Roche for advice on how to optimise future BSH conferences from a pharmaceutical company perspective. This advice was provided during the meeting which took place on the evening of 14 April and was discussed with another active member of the BSH (who was one of health professionals involved in the filming project). It was on this basis that subsistence was provided.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. As stated in the introduction to the Constitution and Procedure, anonymous complaints were accepted and like all complaints, judged on the evidence provided by the parties. Complainants had the burden of proving their complaint on the balance of probabilities. The Panel noted that as the complainant was also non-contactable it was not possible to ask him/her for further information.

Clause 19.1 stated that hospitality must be strictly limited to the main purpose of the event and must be secondary to the purpose of the meeting ie subsistence only. The level of subsistence offered must be appropriate and not out of proportion to the occasion. The supplementary information to Clause 19.1 made it clear that the provision of hospitality was limited to refreshments/subsistence (meals and drinks), accommodation, genuine registration fees and the payment of reasonable travel costs which a company might provide to sponsor a delegate to attend a meeting. In determining whether a meeting was acceptable or not consideration needed to be given to the educational programme, overall cost, facilities offered by the venue, nature of the audience, subsistence provided and the like. It should be the programme that attracted delegates and not the associated hospitality or venue. The supplementary information also stated that a useful criterion in determining whether the arrangements for any meeting were acceptable was to apply the question 'would you and your company be willing to have these arrangements generally known?' The impression that was created by the arrangements for any meeting must always be kept in mind.

The Panel noted that in addition to the requirements in the Code regarding meetings and the provision of hospitality companies were required to have a written document setting out their policies on meetings and hospitality and associated allowable expenditure. The Panel noted that company policies and procedures had to be in line with the Code. A company's policies might be even more restrictive than the Code. It might be that this had contributed to the complainant's concerns.

The Panel noted that the Roche SOP UK meetings and hospitality (UK 107) stated that all meetings must have a clear, substantial and demonstrable educational content. Its appendix, Expenses, stated in the section headed 'Subsistence' that a pre- and post-dinner glass of beer or wine may be provided. When the meeting involved an overnight stay post-dinner drinks (beer, wine or soft drinks) in the hotel bar area could be offered to delegates but this was not obligatory. The most senior member of the Roche team would determine the appropriate level of post-dinner drinks. Roche staff should not remain in the bar with customers later than midnight. After this time Roche attendees should withdraw from the bar. If health professionals continued drinking they must pay for themselves and Roche staff should not be present. The appendix stated that it was unacceptable for any Roche employee to attend clubs and bars with health professionals after a meal or a meeting even if health professionals paid for their own drinks.

The Panel noted that the complainant had alleged that he/she had witnessed on many occasions Roche staff actively entertaining customers and buying drinks at the hotel bar. The Panel noted that Roche had provided a detailed account of subsistence provided during the conference including that

provided at venues other than the bar of the named hotel. The Panel limited its consideration to the subject of the complaint; subsistence provided in the named hotel bar.

The Panel noted that the conference at issue lasted from Monday, 15 April to Wednesday, 17 April. The Panel noted that a Roche meeting to review logistics for the week which took place on Sunday, 14 April in the bar area of the hotel included four health professionals. The health professionals comprised one speaker, two health professionals whom Roche anticipated would take part in the filming of a congress meeting later that week and a health professional who had requested advice from Roche about optimizing future conferences from a company perspective. The latter health professional's attendance at the meeting was not sponsored by Roche and he/she was not providing a service for Roche, such as speaking at a Roche meeting. He/she was a BSH sub-committee member. It was this health professional who also accompanied five Roche employees to a local restaurant for dinner later that evening. Roche submitted that all attendees returned to the hotel and their respective rooms without going to the hotel bar. The Panel noted that in relation to subsistence at the hotel bar, 13 drinks had been provided for 10 individuals over 2 hours and considered that the level of hospitality was not unreasonable in relation to three of the four health professionals involved. The Panel noted that whilst the complaint concerned subsistence provided at the hotel bar, to consider whether this was reasonable in relation to the individual health professional who subsequently accompanied Roche staff to the restaurant, it had to bear in mind the overall level of subsistence provided that evening. In that regard the Panel noted that according to Roche, five employees and one agency member of staff accompanied the health professional concerned to the restaurant. The bill provided by Roche however indicated that there were five people present not seven as submitted by Roche. The bill stated that a 10% service charge would only be added to groups of 6 or more. 10% service charge had been added to the bill. The position was unclear. The bill was for £243.27 including £82.80 for wine.

The Panel was concerned about the subsistence provided to the health professional who was also an active BSH member, on Sunday, 14 April. The Panel noted that the educational content of the conference began the following day. There was thus no educational programme on the day in question and Roche had not argued that the subsistence was secondary to a conference educational event. According to Roche the health professional in question wanted to understand how to optimise conferences from a pharmaceutical company perspective. Whilst it was acceptable for a company to answer such questions it had to ensure that any accompanying subsistence was proportionate; acceptable in relation to the requirements of Clause 19.1 and secondary to the main purpose of the meeting. The Panel noted that subsistence of pre-dinner drinks at the hotel bar followed by a meal at a local restaurant had been provided for what should have been a relatively straightforward discussion. The Panel was concerned about the informal nature of the arrangements including the absence of an agenda bearing in mind the overall level of subsistence provided which included a meal at a restaurant. The company should be able to clearly demonstrate that the subsistence was secondary to the discussion in question. The Panel noted that the complainant bore the burden of proof and further noted, from the introduction to the Constitution and Procedure, that complaints were decided on the evidence provided by the parties. The Panel considered that, bearing in mind all the evidence before it and for the reasons set out above, the subsistence provided to the health professional in question at the hotel bar, noting the overall level of subsistence provided to him/her that evening, was, on balance, contrary to the requirements of Clause 19.1 and a breach of that clause was ruled.

The Panel noted that a group of five Roche staff went to the hotel bar on the evening of Monday, 15 April but were not accompanied by health professionals nor according to Roche were health professionals otherwise present at the bar. On Tuesday, 16 April Roche provided early evening drinks at the hotel bar to, *inter alia*, two health professionals who were speakers for Roche at the conference; £74.40 was spent on 16 drinks for nine people. After dinner that evening at a local restaurant three Roche staff and one health professional returned to the bar and shared a bottle of wine. A group of health professionals who came into the bar shortly afterwards were told that Roche could not purchase a drink for them as they were leaving the bar shortly. The Roche staff did not consume the wine that was then brought for them by one of these health professionals. The Panel noted that whilst the complaint concerned subsistence provided at the hotel bar to consider whether this was reasonable it had to bear in mind the overall level of subsistence provided to the individual health professional who was accompanied by Roche employees throughout the evening. In this regard the Panel noted the restaurant bill for four individuals came to £179.90 including £53.36 for drinks. The Panel considered that bearing in mind the overall level of subsistence provided to this individual throughout the evening, the level of subsistence provided at the bar was not unreasonable.

The Panel noted that it had raised some concerns as set out above and had ruled one matter in breach of the Code. In relation to the subsistence provided to health professionals (other than the one health professional on Sunday, 14 April), the Panel ruled no breach of Clause 19.1 and consequently no breach of Clause 9.1.

Complaint received **7 May 2013**

Case completed **15 July 2013**

CASE AUTH/2604/5/13

NOVO NORDISK v SANOFI

Promotion of Lyxumia

Novo Nordisk complained about a Lyxumia (lixisenatide) advertisement issued by Sanofi and published in the Health Service Journal. Lyxumia was a selective glucagon-like peptide-1 (GLP-1) receptor agonist.

The detailed response from Sanofi is given below.

Novo Nordisk alleged that the emphasis on 'only once-daily' in the claim 'Lyxumia is the only once-daily GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin' was misleading. It implied that Lyxumia was the only once daily GLP-1 receptor agonist available, which was not so. Novo Nordisk also stated that the claim could be read with omission of the word 'and', thereby referring to the use of Lyxumia in combination with oral antidiabetic drugs only. As its product Victoza was also a once-daily GLP-1 receptor agonist for use with oral antidiabetic drugs, it was misleading to use the word 'only' in this context.

The Panel considered that emboldening 'only once-daily' in the claim 'Lyxumia is the only once-daily GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin', implied that Lyxumia was the only once-daily GLP-1 receptor agonist which was not so; Victoza was also a once-daily GLP-1 receptor agonist. Lyxumia and Victoza were both licensed as adjunctive therapy – to be added to existing antidiabetic therapy to achieve improved glycaemic control. Lyxumia could also be added to an existing treatment regimen which included insulin. The Panel accepted that, in the round, this claim was true, but considered that the 'and/or' made it unclear as to what 'only' referred to. Whilst the latter two treatment scenarios were correct in that only Lyxumia could be added to existing insulin therapy, the first was not; both Victoza and Lyxumia could be given to patients not currently controlled on OAD therapy. The Panel considered that the claim was misleading and ambiguous and a breach of the Code was ruled.

Novo Nordisk further alleged that the claims 'Lyxumia leads to even greater costs savings' and 'Turn to the GLP-1 that minimises costs' implied Lyxumia could save costs vs other available treatments. Such a comparison did not take into account the difference in efficacy and safety between similar treatments and was therefore alleged to be misleading, inaccurate and unfair.

In the Panel's view the claim 'Turn to the GLP-1 that minimises costs' would be read as an indirect comparison of Lyxumia with all other GLP-1 receptor agonists. The claim 'Lyxumia leads to even greater cost savings of:' appeared in the body of the advertisement above two stab points which referred respectively to a 26% saving vs Bydureon (exenatide) 2mg once-weekly and Victoza 1.2mg once-daily and a 51% saving vs Victoza 1.8mg once-daily. Without the benefit of more information, it was not clear that the claims were only based on acquisition costs and not a cost-effectiveness analysis or similar. In that regard the Panel considered that the claims as well as the comparisons were misleading and breaches of the Code were ruled.

Novo Nordisk Limited complained about a Lyxumia (lixisenatide) advertisement (ref GBIE.LYX.13.02.11) issued by Sanofi and published in the Health Service Journal, March 2013. Sanofi stated that the advertisement at issue was first used after 5 March 2013, and was withdrawn from use on 29 April 2013 at the conclusion of certain aspects of inter-company dialogue.

Lyxumia was indicated for the treatment of adults with type 2 diabetes to achieve glycaemic control in combination with oral glucose lowering medicines and/or basal insulin when these, together with diet, did not provide adequate glycaemic control. Lixisenatide was a selective glucagon-like peptide-1 (GLP-1) receptor agonist. Novo Nordisk marketed Victoza (liraglutide) which was also a GLP-1 receptor agonist used in the treatment of type 2 diabetes.

1 Claim 'Lyxumia is the *only once-daily* GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin'

This claim appeared beneath the heading 'New Lyxumia 15% cost saving vs Byetta' and was referenced to the Lyxumia summary of product characteristics (SPC).

COMPLAINT

Novo Nordisk stated that the emphasis on the words 'only once-daily' drew the reader to conclude that Lyxumia was the only once daily GLP-1 receptor agonist available, which was not so.

Novo Nordisk also stated that the claim could be read in different ways and highlighted the various combinations for which Lyxumia could be used, namely:

- In combination with oral antidiabetic drugs (OADs) only;
- In combination with basal insulin only;
- In combination with basal insulin and OADs.

In inter-company dialogue Sanofi submitted that the claim accurately reflected the SPC, however, as Novo Nordisk had highlighted, the phrase 'only once-daily' did not feature in the SPC. Sanofi maintained that the claim explicitly and specifically referred to the only once-daily product licensed to be used with basal insulin. While Lyxumia was the 'only' once-daily GLP-1 receptor agonist that could be used in combination with basal insulin, the claim could also be read with omission of the word 'and', thereby referring to the use of Lyxumia in combination with OADs only. As Victoza was also a once-daily GLP-1 receptor agonist licensed to be used in combination with OADs, it was misleading to use the word 'only' within this context.

Novo Nordisk alleged that the claim was misleading in breach of Clause 7.2.

RESPONSE

Sanofi stated that Novo Nordisk alleged that the claim was in breach and that if it was read with a word omitted it would have another meaning, and was therefore misleading.

GLP-1 receptor agonists were used in the treatment of type 2 diabetes and activated the endogenous GLP-1 receptor. Once activated, this receptor acted on multiple pathways serving to reduce circulating glucose concentrations and improve the hyperglycaemia that was characteristic of diabetes.

There were four GLP-1 receptor agonists licensed for use in the UK. Lyxumia and Victoza were the only two indicated to be used once-daily; the other two, Byetta (exenatide) and Bydureon (exenatide LAR) were indicated twice daily or once weekly, respectively.

The Lyxumia SPC stated that it was indicated:

> '... for the treatment of adults with type 2 diabetes mellitus to achieve glycaemic control in combination with oral glucose-lowering medicinal products and /or basal insulin...'

The Victoza SPC stated that the product was indicated:

> '... for treatment of adults with type 2 diabetes mellitus to achieve glycaemic control:
> In combination with:
> – Metformin or a sulphonylurea ...
> – Metformin and a sulphonylurea or metformin and a thiazolidinedione ...'

Sanofi submitted that it was self-evident that the two indications were fundamentally different. It was clear to the reader that Lyxumia had an indication to be used in combination with basal insulin and that this indication did not exist for Victoza. On this basis, Sanofi submitted that it was neither misleading nor inappropriate to reference this fact within materials – it was a genuine point of differentiation between the two medicines. Lyxumia was the only GLP-1 receptor agonist indicated for use in combination with 'oral antidiabetic drugs and/or basal insulin'. The claim was therefore an accurate and truthful representation of the uniqueness of the indication for Lyxumia. The phrase 'only once-daily' was emboldened to emphasise a genuine difference not to claim that Lyxumia was the only once-daily GLP-1 receptor agonist as alleged. If that were implied, all these words would be emboldened. Regardless, the sentence needed to be considered in its entirety and this was an accurate representation of a unique indication for the product.

In summary, Lyxumia was the only GLP-1 receptor agonist available that was indicated for use once-daily with oral antidiabetic agents and/or basal insulin, the claim was an accurate representation of the uniqueness of Lyxumia's indication, and was not misleading.

Novo Nordisk invited the claim to be read with a word omitted. The claim however was to be read as written, and Sanofi had responded to the claim as written. Novo Nordisk presented a fallacious argument – it was completely illogical to suggest that the indication for Victoza (in combination with oral agents) was the same as that for Lyxumia because it matched one of the three ways in which the latter was indicated. To ignore the fact that Lyxumia was also indicated for use in combination with basal insulin, or in combination with oral agents plus basal insulin, could not be negated by this approach. The indication for Lyxumia, when considered in total (as reflected in the advertisement), was unquestionably different from that of Victoza. Sanofi submitted it was not misleading to position Lyxumia as unique in that respect.

PANEL RULING

The Panel noted the claim at issue 'Lyxumia is the **only once-daily** GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin'. The Panel considered that by emboldening 'only once-daily' there was an implication that Lyxumia was the only once-daily GLP-1 receptor agonist which was not so; Victoza was also a once-daily GLP-1 receptor agonist. Lyxumia and Victoza were both licensed as adjunctive therapy – to be added to existing antidiabetic therapy to achieve improved glycaemic control. Both medicines could be added to existing OAD therapy but only Lyxumia could also be added to an existing treatment regimen which included insulin. The Panel considered that the use of 'and/or' in the claim did not make this distinction between the two medicines entirely clear. The claim meant that Lyxumia was the only once-daily GLP-1 receptor agonist that was licensed for use in patients not optimally controlled on OADs, not optimally controlled on OADs and basal insulin and not optimally controlled on basal insulin alone. The Panel accepted that, in the round, this claim was true, but considered that the 'and/or' made it unclear as to what 'only' referred to. Whilst the latter two treatment scenarios were correct in that only Lyxumia could be added to existing insulin therapy, the first was not; both Victoza and Lyxumia could given to patients not currently controlled on OAD therapy. The Panel considered that the claim

was misleading and ambiguous. A breach of Clause 7.2 was ruled.

2 Claims 'Lyxumia leads to *even greater costs savings* of:' and 'Turn to the GLP-1 that minimises costs'

COMPLAINT

Novo Nordisk alleged that both of these claims implied Lyxumia could save costs vs other available treatments within the same class. While these claims were correct when the pack price of Lyxumia was compared to the pack price of other similar treatments, this comparison did not take into account the differences in efficacy and safety between similar treatments. While the advertisement included comparative efficacy and safety data between Lyxumia and twice daily exenatide to support a cost saving claim, Sanofi failed to include comparative data vs Victoza when making the same cost saving claim. Kapitza *et al*, (2013) demonstrated that Victoza provided 60% better reduction in HbA_{1c} levels and 50% better weight reduction vs Lyxumia over a 4 week period. True cost savings which were meaningful to health professionals and payers could not be based on pack price alone, but instead must take into account comparative efficacy and safety data in order for long-term cost savings to be realised.

As stated within the supplementary information to Clause 7.2, 'price comparisons, as with any comparison, must be accurate, fair and must not mislead. Valid comparisons can only be made where like is compared with like'.

In inter-company dialogue Sanofi acknowledged that cost saving comparisons might invite conclusions beyond acquisition cost and committed to amend such claims. Novo Nordisk considered this matter closed. Two days later, on 1 May 2013, Sanofi issued a press release (ref GBIE.LYX.13.03.12, available on www.sanofi.co.uk) to launch Lyxumia. Various cost saving claims were made in the press release in relation to Lyxumia, without naming or providing any information on the comparative efficacy and safety of similar available treatments. Claims included:

- 'Costing 25% less than similar treatments …'
- A quotation 'It is encouraging that effective and innovative Type 2 diabetes treatments are made available more cheaply to the NHS and the patients it treats'
- A quotation: 'The price is one that represents real value to both the NHS and Sanofi'.

As the press release was embargoed until 00.01 on Wednesday, 1 May 2013, and given the impact such a release could have, Novo Nordisk's considered that Sanofi had had time to amend the cost saving claims in light of its commitment made to Novo Nordisk on 29 April in relation to cost saving claims in the Health Service Journal advertisement.

Novo Nordisk alleged that the claims 'Lyxumia leads to even greater costs savings' and 'Turn to the GLP-1 that minimises costs' were misleading, inaccurate and unfair comparisons, in breach of Clauses 7.2 and 7.3.

RESPONSE

Sanofi stated that whilst Lyxumia was the cheapest GLP-1 receptor agonist available in the UK (15% cheaper than exenatide 10mcg twice daily, 26% cheaper than exenatide 2mg weekly and Victoza 1.2mg daily, 51% cheaper than Victoza 1.8mg daily), Sanofi understood as how these claims might be considered to imply wider savings than the cost of the medicine alone. This was not intended, but taking into account this concern the advertisement was withdrawn from further use. Sanofi had honoured a commitment not to use these claims further.

With respect to the advertisement at issue, Sanofi considered that inter-company dialogue reached a definitive conclusion. The advertisement was withdrawn and claims of 'cost saving or cost minimisation' had not been used again. In respect to these actions Sanofi therefore submitted that all the requirements of the Code had been upheld.

Sanofi was therefore exceedingly disappointed that Novo Nordisk had referred the matter to the PMCPA after an apparently successful resolution, at the very least without any further recourse to inter-company discussion in an attempt to resolve any new concerns.

Although Novo Nordisk referred to new claims that appeared in a subsequent press release, Novo Nordisk had not complained to Sanofi or the PMCPA about the item itself. Although no complaint has been made, Sanofi was confident that the content of the press release could be substantiated and met the requirements of the Code, and it would defend these points rigorously were such a complaint forthcoming.

Before it was issued the press release was examined to ensure that the commitment mentioned above was respected. No explicit nor implicit claim that Lyxumia would achieve 'cost savings' or 'cost minimisation' beyond the cost of the medicine itself was made. Instead, the press release reflected the fact that Lyxumia was cheaper than the other GLP-1 receptor agonists at the equivalent dosage for the same indication, as required by Clause 7.2. The quotations from the press release cited by Novo Nordisk reflected the simple message of cheaper cost; not one implied the potential to achieve savings beyond the cost of the medicine alone. The quotations simply reported that Lyxumia cost '… less than similar treatments …' or was available '… more cheaply to the NHS …'.

In summary, Sanofi agreed with Novo Nordisk that the advertisement at issue could have been interpreted more widely than intended, and withdrew it as a consequence of inter-company dialogue. At the same time a commitment was given that further claims regarding the cheaper cost would avoid any such ambiguity. Sanofi considered that

inter-company dialogue had reached a successful conclusion with respect to this item and these claims.

For Novo Nordisk now to introduce a matter, upon which Sanofi had had no opportunity to comment, was disappointing. Sanofi recognised that the complaint had been made only in reference to the original journal advertisement. Regardless, Sanofi would be willing to respond to Novo Nordisk regarding any element of the press release, but would expect the first approach to be in the form of inter-company dialogue as required by the Code.

Sanofi looked forward to receiving the Panel's conclusion regarding the advertisement in due course, albeit that the advertisement was already withdrawn and the company's commitment made (and respected) not to repeat potentially ambiguous claims in the future.

PANEL RULING

The Panel noted that in a letter to Novo Nordisk dated 29 April, Sanofi had agreed that the cost saving comparison in the advertisement at issue might invite conclusions beyond acquisition cost alone and had committed to amend the claim. Sanofi had also acknowledged Novo Nordisk's concerns about the comparison with Victoza. Sanofi stated in that letter that it had instructed its agency not to use the advertisement forthwith. The Panel further noted, however, that a press release which was embargoed until 00.01, Wednesday 1 May featured the claim 'Lyxumia is a new, cost-effective option….'. The Panel thus disagreed with Sanofi's submission that the press release made no explicit or implicit claim that Lyxumia would achieve 'cost savings' or 'cost minimisation' beyond the cost of the medicine itself. The Panel considered that the term 'cost-effective' clearly implied savings beyond the acquisition cost alone and in that regard inter-company dialogue had been unsuccessful and the matter should proceed.

The Panel noted that the claim 'Turn to the GLP-1 that minimises costs' appeared in bold, dark type in the bottom left-hand corner of the advertisement. In the Panel's view the claim would be read as an indirect comparison of Lyxumia with all other GLP-1 receptor agonists. The claim 'Lyxumia leads to *even greater cost savings* of:' appeared in the body of the advertisement above two stab points which referred respectively to a 26% saving vs Bydureon (exenatide) 2mg once-weekly and Victoza 1.2mg once-daily and a 51% saving vs Victoza 1.8mg once-daily. The Panel considered that without the benefit of more information, it was not clear that the claims were only based on acquisition costs and not a cost-effectiveness analysis or similar. In that regard the Panel considered that the claims were misleading and a breach of Clause 7.2 was ruled. The comparisons were thus also misleading and a breach of Clause 7.3 was ruled. The Panel noted that the advertisement had already been withdrawn.

Complaint received **13 May 2013**

Case completed **26 June 2013**

CASE AUTH/2609/6/13

VOLUNTARY ADMISSION BY ROCHE

Failure to sit ABPI Medical Representatives Examination

Roche Products voluntarily advised the Authority that one of its promotional employees had not taken the ABPI Medical Representatives Examination, in breach of the Code. The employee had originally undertaken a non-promotional role but moved into a promotional role (relations manager) in December 2010.

In accordance with Paragraph 5.6 of the Constitution and Procedure for the Prescription Medicines Code of Practice Authority, the Director treated the matter as a complaint.

The detailed response from Roche is given below.

The Panel noted that the employee at issue had started the promotional role in December 2010 and in May 2013 had not yet taken the ABPI Medical Representatives Examination.

The Panel noted that the employee's role and responsibilities, as acknowledged by Roche, satisfied those of a representative as set out in the Code. The employee had not passed the examination contrary to the requirements of the Code. A breach of the Code was ruled as acknowledged by Roche.

The Panel noted that Roche had no process for checking the ABPI examination status of staff that transferred roles within the company and the error was only identified due to a complaint about another matter. In that regard the Panel considered that the company had not maintained high standards and a breach of the Code was ruled. Although concerned about Roche's lack of process, the Panel ruled no breach of Clause 2.

Roche Products Limited voluntarily advised the Authority that one of its promotional staff members had not taken the ABPI Medical Representatives' Examination. Roche submitted that it had failed to check the ABPI examination status of the employee when they had transferred roles internally within the company.

In accordance with Paragraph 5.6 of the Constitution and Procedure for the Prescription Medicines Code of Practice Authority, the Director treated the matter as a complaint.

COMPLAINT

Roche stated that during its investigation in order to respond to Case AUTH/2603/5/13, it discovered that one of its employees in a promotional role (relations manager) had not taken the ABPI Medical Representatives Examination.

The employee had originally been engaged by Roche in a non-promotional role. In December 2010 she moved to the position of relations manager. A copy of the job description was provided.

Roche stated that the employee's role was field-based but unusually reported to a head office manager. The normal process to verify the ABPI qualification of a field-based role was undertaken by the field-based manager. Roche noted that unfortunately due to the unusual reporting line, the check had not taken place in this case.

Roche immediately instructed its employee to cease all promotional activity and the employee had now been transitioned to another non-promotional role.

Roche submitted that it had failed to comply with the requirements of Clause 16.3 and to maintain high standards in breach of Clause 9.1 because it had not checked the ABPI examination status of the employee in question when the employee had moved from a non-promotional to a promotional role. Roche recognised that given the length of time its employee had been in a promotional role before the error was discovered the Panel might want to consider Clause 2.

In summary, Roche recognised the seriousness of the omission but considered that it had, upon discovery of the oversight, acted immediately and appropriately to address the issue. Roche submitted that the relations manager job description would be revised to ensure it was clear that success in the ABPI Medical Representatives Examination was a requirement of the role. The current job description provided listed ABPI qualified under desirable knowledge and experience.

When writing to Roche, the Authority asked it to respond in relation to Clauses 2, 9.1 and 16.3 of the Code.

RESPONSE

Roche provided a copy of its standard operating procedure (ABPI Code SOP UK 112 Representatives Training) which outlined the process regarding checking the ABPI examination status of relevant employees.

Roche required its representatives (including contract representatives) to pass the appropriate ABPI examination in line with the Code. The requirement extended to sales managers and suchlike whose duties comprised or included either calling upon doctors and/or other prescribers (albeit as business managers within the NHS) and/or the

promotion of medicines on the basis, *inter alia*, of their therapeutic properties (which also included discussions around cost).

The SOP noted that representatives were accountable for providing the human resources/ recruiting manager or initial training course coordinator with a copy of their ABPI examination certificate. Human resources was accountable for keeping records of ABPI examination results and certificates, flagging those who had not passed the examination to the training department and terminating the contracts of those who did not pass the examination within the appropriate time limit.

Roche submitted that if an existing employee moved from a non-promotional to a promotional role, as in this case, human resources confirmed that the process was for the head office assessment team to check the ABPI examination status of head office-based roles and field-based line managers to check the status of field-based roles. However, this process was not documented.

Roche noted that the relations manager was a field-based role that reported in to a head office manager. The normal verification of the ABPI qualification of a field-based role was undertaken by the field-based manager, as described above. Unfortunately in this case, due to the role reporting into a head office-based position rather than a field-based manager, the check had not taken place.

Roche confirmed that it discovered the lack of an ABPI examination qualification for the individual whilst investigating the complaint in Case AUTH/2603/5/13, wherein the Authority asked whether Roche staff who had paid for hospitality for health professionals at a UK congress had passed the ABPI examination.

On discovering this oversight, Roche immediately instructed the employee in question to cease all promotional activity and the employee had now moved to a non-promotional role. In addition the ABPI examination status of all Roche relations managers had been checked and Roche confirmed that all (except the individual in question) had successfully completed the ABPI examination.

With regard to the clauses raised in this voluntary admission, Roche submitted that it had failed to comply with the requirements of, and was therefore in breach of, Clause 16.3. In addition, Roche considered that, given the length of time that its employee in question was in a promotional role before this error was discovered, it had failed to maintain high standards and was therefore in breach of Clause 9.1.

Roche considered that, on discovering this error, it acted swiftly and appropriately to address the situation by instructing its employee to cease all promotional activity. In addition, Roche had verified the ABPI examination status of the remaining relations managers as successfully completed and would revise its representative training SOP to ensure that checks of this status for internal moves into a promotional role were performed with the same rigour as those for new employees beginning a promotional role. Roche had no further comments in relation to the requirements of Clause 2 beyond that set out above.

PANEL RULING

The Panel noted that Clause 16.3 stated that representatives must pass the appropriate ABPI representatives examination. They must take the appropriate examination within their first year of such employment. Prior to passing the appropriate examination, they might be engaged in such employment for no more than two years, whether continuous or otherwise. The relevant supplementary information gave the Director discretion to grant an extension in the event of failure to comply with either time limit subject to the representative taking or passing the examination within a reasonable time.

The Panel noted that a representative was defined in Clause 1.6 as someone who called on members of the health professions and administrative staff in relation to the promotion of medicines. In the Panel's view such people would often have job titles other than 'representative'. The term promotion was defined in Clause 1.2 as any activity undertaken by a pharmaceutical company or with its authority which promoted the administration, consumption, prescription, purchase, recommendation, sale, supply, or use of its medicines. Clause 16.4 stated that the ABPI Medical Representatives Examination must be taken by representatives whose duties comprised or included one or both of calling upon, *inter alia*, doctors and/or other prescribers; and/ or the promotion of medicines on the basis of their particular therapeutic properties.

The Panel noted that the relations manager, had started in that role in December 2010 and in May 2013 had not yet taken or passed the ABPI Medical Representatives Examination.

The Panel noted that certain performance standards/ indicators of the relations manager role referred to 'marketing strategy, 'promotional objectives' and 'product information in line with strategy'. In that regard, the Panel considered that the role and responsibilities of the relations manager as acknowledged by Roche satisfied those of a representative set out in the Code (Clauses 1.6 and 16.4). The relations manager had not passed the examination contrary to the requirements of the Code and a breach of Clause 16.3 was ruled as acknowledged by Roche.

The Panel considered that the failure of the relations manager to pass the ABPI Medical Representatives Examination despite the fact the company's SOP required such an employee to do so was because the company had no process for checking the ABPI examination status of staff who transferred roles within the company. The Panel also noted that the error was only identified due to a complaint about another matter. The Panel considered that the lack of process amounted to a failure to maintain high standards and ruled a breach of Clause 9.1.

The Panel was concerned about Roche's lack of process to check the ABPI examination status of staff transferring roles internally within the company. However, taking all of 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.

Complaint received **7 June 2013**

Case completed **11 July 2013**

CODE OF PRACTICE REVIEW – August 2013

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

2572/1/13	Ex-employee v AstraZeneca	Promotion of Seroquel	No breach	Appeal by complainant	Page 3
2573/1/13	Ex-employee v Gedeon Richter	Sponsorship to attend an international meeting	No breach	No appeal	Page 15
2574/2/13	**Pharmacist v Sanofi Pasteur MSD**	**Promotion of Zostavax**	**Breach Clause 9.1**	**No appeal**	**Page 17**
2575/2/13	**Ex-employee v Gedeon Richter**	**Promotion of Esmya**	**Breaches Clauses 2 and 3.1** **Two breaches Clause 9.1** **Breaches Clauses 14.2 and 19.1**	**No appeal**	**Page 21**
2576/2/13	**Anonymous General Practitioner v Abbott**	**Promotion of Hidrasec including via social media**	**Breaches Clauses 9.1, 22.1 and 22.2**	**No appeal**	**Page 28**
2580/2/13	**Ex-employee v Gedeon RIchter**	**Meeting invitation**	**Breach Clause 4.1**	**Appeal by complainant**	**Page 33**
2581/2/13	**Lilly and Boehringer Ingelheim v Merck Sharp & Dohme**	**Promotion of Januvia**	**Breaches Clauses 7.2, 7.8, 7.3 and 9.1**	**No appeal**	**Page 37**
2583/3/13	**Almirall v Leo**	**Picato advertisement**	**Two breaches Clause 7.10** **Breach Clause 9.1**	**No appeal**	**Page 42**
2584/3/13	Pharmacist v Almirall	Invitation to a meeting	No breach	No appeal	Page 45
2586/3/13	**Voluntary admission by Ferring**	**Symposium flyers**	**Two breaches Clause 14.1**	**No appeal**	**Page 47**
2587/3/13	Anonymous Gastroenterology consultant v Almirall	Free stock allegedly offered as an inducement	No breach	No appeal	Page 50
2588/3/13	**The Drug and Therapeutics Bulletin v Novartis**	**Promotion of Seebri Breezhaler**	**Three breaches Clauses 7.2** **Two breaches Clause 7.4** **Breach Clause 9.1**	**No appeal**	**Page 53**
2589/3/13	Pharmacosmos/ Director v Vifor	Alleged breach of undertaking	No breach	No appeal	Page 58
2591/3/13	**Anonymous v Merck Serono**	**Conduct of representative**	**Breach Clause 15.9**	**No appeal**	**Page 61**
2592/4/13	**Voluntary admission by GlaxoSmithKline**	**Benlysta case studies**	**Breaches Clauses 3.2, 4.1, 7.2, and 14.1**	**No appeal**	**Page 64**
2594/4/13	General Practitioner v Lundbeck	Email promotion of Cipralex	No breach	No appeal	Page 67
2595/4/13	**Pharmacist v Lilly**	**Promotion of Alimta**	**Three breaches Clause 7.2** **Breach Clause 7.4**	**No appeal**	**Page 69**

2596/4/13	Almirall/Director v Leo	Alleged breach of undertaking	No breach	No appeal	Page 71
2598/4/13	**Consultant Rheumatologist v Roche**	**Promotion of Mabthera**	**Breaches Clauses 3.2 and 9.1**	**No appeal**	**Page 73**
2599/4/13	Anonymous v Merck Sharp & Dohme	Cerazette rebate scheme	No breach	No appeal	Page 76
2601/5/13	**Ex-employee/ Director v Gedeon Richter**	**Breach of undertaking**	**Breaches Clauses 2, 9.1 and 25**	**No appeal**	**Page 78**
2602/5/13	Anonymous v Chugai	Provision of hospitality	No breach	No appeal	Page 80
2603/5/13	**Anonymous v Roche**	**Provision of hospitality**	**Breach Clause 19.1**	**No appeal**	**Page 84**
2604/5/13	**Novo Nordisk v Sanofi**	**Promotion of Lyxumia**	**Two breaches Clause 7.2** **Breach Clause 7.3**	**No appeal**	**Page 89**
2609/6/13	**Voluntary admission by Roche**	**Failure to sit ABPI Medical Representatives Examination**	**Breaches Clauses 9.1 and 16.3**	**No appeal**	**Page 93**

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
by email to: complaints@pmcpa.org.uk.