NUMBER 77 August 2012

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.

PMCPA WEBSITE

The new improved website was launched in August. The response has been very positive so far. Thank you to all those involved in its development, particularly those from companies who user tested the site and provided detailed comment prior to launch.

Please continue to let us have your feedback on the site.

SECOND 2012 EDITION OF THE CODE

The Second 2012 Edition Code came into effect on 1 July 2012 and has a transitional period until 31 October 2012. During this time no promotional material or activity will be regarded as being in breach of the Code if it fails to comply with its provisions only because of newly introduced requirements. Printed copies are now available. Details of the amendments are available on the PMCPA website. The changes were due to the new IFPMA Code of Practice which came into operation on 1 September 2012 and the new UK legislation, The Human Medicines Regulations 2012 which were published in August.

The PMCPA will shortly launch an update of the e-learning module, the quick guides and other publications.

ANNUAL REPORT FOR 2011

The Annual Report of the Prescription Medicines Code of Practice Authority for 2011 has now been published and copies will be sent to all who are on the mailing list for the Code of Practice Review. Further copies are available on request.

There were 84 complaints in 2011 compared with 86 complaints in 2010. There were 92 complaints in 2009.

The 84 complaints in 2011 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complaints involve more than one respondent company and some complaints do not become cases at all because they are withdrawn.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 259 rulings made by the Code of Practice Panel in 2011, 223 (86%) were accepted by the parties, 15 (6%) were unsuccessfully appealed and 21 (8%) were successfully appealed. This compares with the 7% of rulings which were successfully appealed in 2010.

The number of complaints made by health professionals in 2011 exceeded the number made by pharmaceutical companies, there being 30 from health professionals and 22 from pharmaceutical companies. This has historically been the usual pattern although in 1996, 1999, 2001, 2002, 2003 and 2010 the reverse was true.

The average time to deal with all cases in 2011 was 8.8 weeks (10 weeks in 2010). There was a decrease in the time taken for cases settled at the Panel level, 7 weeks in 2011 (8 weeks in 2010) and cases which were appealed, 15 weeks in 2011 (16.9 weeks in 2010).

The Authority advertises brief details of all cases 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 act as a sanction and highlight what constitutes a serious breach of the Code.

Four such advertisements were placed in the BMJ, The Pharmaceutical Journal and the Nursing Standard in 2011.

Copies of the advertisements are on the PMCPA website.

TWEETS AND THE SCOPE OF THE CODE

The Authority has recently received a number of complaints about tweets issued by an overseas parent or affiliate company of a UK pharmaceutical company where the proceedings concluded with the Code of Practice Panel ruling no breach of the Code as the tweets did not come within the scope of the Code.

Under the Constitution and Procedure if a matter is ruled to be outwith the scope of the Code no case report is published (Paragraph 7.6 refers), but we considered it would be helpful to publish informal guidance. The cases in question were only considered by the Panel. The Code of Practice Appeal Board has the last word as to whether material or activities breach the Code.

Clause 24.2 states that information or promotional material about prescription only medicines which is placed on the Internet outside the UK would be regarded as coming within the scope of the Code if it was placed there by a UK company or an affiliate of a UK company or at the instigation or with the authority of such a company and it specifically referred to the availability or use of the medicine in the UK.

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

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

Monday, 24 September

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

For further information regarding any of the above, please contact Nora Alexander for details (020 7747 1443 or email 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 email 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
Ros Henley: 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.

TWEETS AND THE SCOPE OF THE CODE CONTINUED…

The recent cases concerned the activities of the global head offices of pharmaceutical companies; the global offices were not based in the UK. The Panel decided that as a non-UK company had registered the Twitter accounts in question and the UK affiliate had no role in the generation, approval or publication of tweets on the account, or any material linked to the tweets and did not direct a UK audience to the account and as neither the tweets nor any linked material specifically referred to the use of prescription only medicines in the UK, then the tweets and linked material were not covered by the requirements of Clause 24.2. Consequently the tweets and linked material did not come within the scope of the Code.

The tweets would be covered by a code of practice which is likely to be that which applies to the country where the parent company or affiliate generating the tweets resides.

CASE AUTH/2475/1/12

PFIZER v JOHNSON & JOHNSON

Nicorette Invisi Patch leavepiece

Pfizer complained about a leavepiece for Nicorette Invisi 25mg Patch (transdermal nicotine replacement therapy (NRT)) distributed by Johnson & Johnson. Nicorette Invisi 25mg Patch was indicated to aid smokers wishing to quit or reduce prior to quitting, to assist smokers who were unwilling or unable to smoke, and as a safer alternative to smoking for smokers and those around them. Pfizer produced Champix (varenicline) which was indicated for smoking cessation.

The detailed response from Johnson & Johnson is given below.

A table compared a number of qualities of Nicorette Invisi Patch with those of varenicline. The quality 'Indicated as a Safer Option to Smoking' was followed by a green tick ('may be suitable') for the Invisi Patch and a red cross ('not recommended') for varenicline. Pfizer alleged that this implied that it was safer to continue smoking than to try to stop with varenicline. Pfizer alleged that the material was unbalanced, misleading, could not be substantiated, disparaged varenicline and did not demonstrate high standards. Pfizer further noted the statement below the table, 'The varenicline SPC [summary of product characteristics] states: "Care should be taken with patients with a history of psychiatric illness…"' but submitted that there were also a number of special warnings and precautions that were listed in the Nicorette Invisi Patch SPC. Pfizer alleged that data had therefore been 'cherry picked' from the SPCs. Pfizer alleged that the presentation of the information was again misleading, did not present a fair and balanced representation of the safety evidence available and did not demonstrate high standards.

The Panel considered that the table gave the misleading impression that the risk:benefit ratio for varenicline was such that it was safer to continue to smoke than try to quit with varenicline. A breach of the Code was ruled. The comparison of the two medicines was thus also misleading and a breach was ruled. The implication that varenicline was not indicated as a safer alternative to smoking was not capable of substantiation, disparaged varenicline and did not reflect the available evidence regarding the risk:benefit ratio. Breaches were ruled. The Panel considered that the material did not maintain high standards and ruled a breach of the Code. All of these rulings were appealed and in its consideration of the matter the Appeal Board noted the differences between the licensed indications for the medicines and Johnson & Johnson's submission that 'indicated' in the table had been used in its regulatory sense. According to the table, however, a green tick in the Invisi Patch column would be interpreted by the target audience as meaning the product 'may be suitable' as a safer option to smoking and a red cross for varenicline would inevitably be interpreted as meaning the opposite. The Appeal Board considered that the table was misleading as alleged and upheld all of the Panel's rulings.

Turning to the statement below the table that the varenicline SPC stated 'Care should be taken with patients with a history of psychiatric illness…', the Panel noted that this statement was taken from the varenicline SPC. The Panel also noted that although there were a number of warnings listed in the Nicorette Invisi 25mg Patch SPC, there was no warning in relation to use in patients with a history of psychiatric illness. The Panel considered that the statement about varenicline was not misleading with regard to the safety profile of either medicine and that it reflected the available evidence in relation to the use of the medicines in this patient population. No breaches of the Code were ruled including no breach in relation to the maintenance of high standards.

Pfizer alleged that to describe the safety profile of NRT as 'excellent' over-claimed the safety profile of the Invisi Patch in breach of the Code. A bar chart entitled 'Adverse drug reactions in an independent study comparing NRT (all forms) and varenicline', referenced to Stapleton *et al* (2008), depicted a selection of 'adverse drug reactions' from the study. Pfizer stated that with no description of the study design, readers might assume that this was a randomised, head-to-head, clinical trial comparison between NRT and varenicline rather than an observational, non randomised, cohort study which compared a group of patients taking NRT prior to the availability of varenicline, with a different group of patients who were treated with varenicline immediately post-launch. The reporting of adverse events in these cohorts could not imply causality (the term 'adverse drug reactions' should not be used) and the reporting rate for varenicline was likely to be influenced by the proximity to launch. Pfizer alleged that the bar chart was misleading and did not fully describe the design or the findings of the study. It did not allow readers to fully assess the data presented. The safety comparisons made could not be robustly substantiated by Stapleton *et al* and high standards had not been maintained, in breach of the Code.

The Panel noted that the bar chart was on a page headed 'NRT is well tolerated and has an excellent safety profile'. The depicted study, Stapleton *et al*, was concluded before the Nicorette Invisi 25mg Patch was first authorized in December 2008.

The Panel noted Johnson & Johnson's submission that the page at issue was about the safety and tolerability of NRT in general, and not Nicorette

compared with varenicline. The Panel considered, however, that the majority of readers would assume that the results shown in the bar chart were from a comparison of the Invisi Patch with varenicline. This impression was strengthened by the claim below the bar chart 'The favourable safety and tolerability profile of Nicorette has been shown in more than 100 clinical studies'.

The Panel noted that when varenicline was introduced in to the study detailed in Stapleton *et al* it would have been a new medicine. In this regard the Panel considered that patients were more likely to report possible adverse effects with it.

The Panel noted its concerns about the design and timing of the Stapleton study in relation to the availability of the medicines concerned. Within a Nicorette Invisi 25mg Patch leavepiece, the heading 'NRT is well tolerated and has an excellent safety profile' would be read as a claim for Nicorette Invisi 25mg Patch. The Panel considered that Stapleton *et al* did not support such a claim and in that regard the properties of the Invisi Patch had not been presented objectively. A breach of the Code was ruled.

With regard to the bar chart the Panel considered that for the reasons described above in relation to Stapleton *et al* the comparisons depicted were misleading with regard to the Nicorette Invisi 25mg Patch and varenicline. Breaches of the Code were ruled which were upheld on appeal. The bar chart did not present data in such a way as to give a clear and balanced view of the safety profile of either product and the Panel ruled a breach of the Code. As Nicorette Invisi 25mg Patch was not available at the time of the Stapleton *et al* evaluation, the Panel did not consider that the incidence of side-effects presented in the bar chart were capable of substantiation in relation to Nicorette Invisi 25mg Patch. Breaches of the Code were ruled which were upheld on appeal. The Panel considered that the use of the Stapleton *et al* data in this way amounted to a failure to maintain high standards and ruled a breach of the Code which was upheld on appeal.

The back page of the leavepiece was headed 'Nicorette Invisi 25mg Patch – Designed for first line recommendation'. Under a sub-heading 'Designed for tolerability' was the bullet point 'Well tolerated with an excellent safety profile' which was referenced to Tønnesen *et al* (1999). The Panel noted that the treatment used in this study was Nicorette 10mg and 15mg patches and not the Nicorette Invisi 25mg Patch, although some patients received 25mg of nicotine by using both the 15mg and 10mg patches at the same time. The authors concluded that NRT appeared to have few side-effects.

The Panel noted that from the list of six possible adverse events given in the Nicorette Invisi 25mg Patch SPC, one was very common (itching), three were common (dizziness/headache, gastrointestinal discomfort/nausea/vomiting and erythema), two were uncommon (palpitations and urticaria) and one was very rare (reversible atrial fibrillation). The SPC also stated that about 20% of Nicorette Invisi Patch users experienced mild local skin reactions during the first weeks of treatment. The SPC stated that at recommended doses the Nicorette Invisi 25mg Patch had not been found to cause any serious adverse effects. The Panel noted that the claim at issue appeared on the final page of the leavepiece and summarized the data within. The Panel noted its rulings above of breaches of the Code in relation to misleading safety comparisons within the leavepiece. The Panel considered that the claim was not a fair summation of the safety data within which was misleading and thus overclaimed the safety profile of Nicorette Invisi 25mg Patch as alleged. A breach of the Code was ruled.

Pfizer Limited complained about a six page, gate folded leavepiece for Nicorette Invisi 25mg Patch (transdermal nicotine replacement therapy (NRT)) (ref 06491) distributed to prescribers by Johnson & Johnson Limited. Nicorette Invisi 25mg patch relieved and/or prevented craving and nicotine withdrawal symptoms associated with tobacco dependence. It was indicated to aid smokers wishing to quit or reduce prior to quitting, to assist smokers who were unwilling or unable to smoke, and as a safer alternative to smoking for smokers and those around them. Pfizer produced Champix (varenicline) which was indicated for smoking cessation.

The leavepiece, which was no longer in use, had been used and left with prescribers at the end of a product detail.

1 Page comparing Nicorette Invisi 25mg Patch with varenicline

COMPLAINT

Pfizer noted that one page of the leavepiece, entitled 'Nicorette Invisi 25mg Patch - Designed for versatility' with the sub-heading 'Suitable for a wide range of patient situations', featured a table which compared a number of qualities of Nicorette Invisi Patch with those of varenicline. The quality 'Indicated as a Safer Option to Smoking' was followed by a green tick for the Invisi Patch and a red cross for varenicline. Pfizer acknowledged that although the Invisi Patch was indicated as a safer alternative to smoking, the presentation of the information in the table was such as to suggest that the use of varenicline was not a safer alternative to smoking and imply that it was safer to continue smoking than to try to stop with varenicline. Pfizer alleged that the material was unbalanced, misleading, could not be substantiated, disparaged varenicline and did not demonstrate high standards in breach of Clauses 7.2, 7.3, 7.4, 7.9, 8.1 and 9.1.

Pfizer further noted that below the table was the statement 'The varenicline SPC [summary of product characteristics] states: "Care should be taken with patients with a history of psychiatric illness…"'. Whilst this wording was in Section 4.4 (Special warnings and precautions for use) of the varenicline SPC, there were also a number of special warnings

and precautions that were listed in the Nicorette Invisi Patch SPC. For example, caution in underlying cardiovascular disease, diabetes mellitus, phaeochromocytoma and uncontrolled hyperthyroidism had not been included on this page of the leavepiece. Pfizer alleged that data had therefore been 'cherry picked' from the SPCs, that the presentation of the information was again misleading, that it did not present a fair and balanced representation of the safety evidence available and did not demonstrate high standards in breach of Clauses 7.2, 7.9 and 9.1.

RESPONSE

Johnson & Johnson submitted that the table at issue was intended to allow prescribers to review and compare situations and patient groups where Nicorette Invisi Patch or varenicline would be appropriate. It was drawn from Sections 4.1, Therapeutic indications, 4.3, Contraindications, 4.6, Pregnancy and lactation and 4.7, Effects on ability to drive and use machines, of the SPCs. Johnson & Johnson considered it was a fair reflection of the situations where the two products might or might not be appropriate for use.

The indication section of the Nicorette Invisi 25mg Patch SPC stated: 'It is indicated to aid smokers who wish to quit or reduce prior to quitting, to assist smokers who are unwilling or unable to smoke, and as a safer alternative to smoking for smokers and those around them' (emphasis added). Johnson & Johnson submitted that 'safer alternative to smoking' was a specific indication. It did not simply mean that using the product was safer than smoking, it meant that it could be used when the smoker did not intend to quit but wished to reduce risk to themselves or those around them. By contrast, varenicline did not include this specific indication. Johnson & Johnson submitted that it had expressed this as 'safer option to smoking' rather than 'safer alternative to smoking' in its communications because although the two phrases meant the same, 'a safer option' communicated the nature of the indication clearly and accessibly. The word 'indicated' was specifically included in the description to make this meaning clear and to avoid any doubt.

Johnson & Johnson did not consider that placing a tick against its indication in the table was unbalanced, misleading, could not be substantiated, disparaged varenicline or failed to demonstrate high standards and thus denied breaches of Clauses 7.2, 7.3, 7.4, 7.9, 8.1 and 9.1.

In relation to the statement 'Care should be taken with patients with a history of psychiatric illness…', Johnson & Johnson submitted that this was a direct and accurate quote from the varenicline SPC. It was a topic which had received considerable publicity, had been the subject of a CHM (Commission on Human Medicines) labelling change and was sufficiently important to be included in the comparison between NRT and varenicline. It was not included to mislead, present an unbalanced picture or to disparage varenicline. Varenicline was a licensed medicine and as such had a positive risk:benefit ratio and an established place in smoking cessation. The page in question was intended to allow the prescriber to think about situations where use of the medicine might be more or less appropriate, and clearly a history of psychiatric illness was a relevant consideration for prescribers.

Johnson & Johnson did not consider that the inclusion of this claim was misleading or failed to present a fair balanced representation of safety evidence or that it failed to demonstrate high standards, and in its view it did not breach Clauses 7.2, 7.9 or 9.1.

PANEL RULING

The Panel noted that in the table comparing various qualities of the Invisi Patch with those of varenicline, the quality 'Indicated as a Safer Option to Smoking' had a green tick in the Nicorette column and a red cross in the varenicline column. Below the table it was stated that the red cross indicated that the medicine was not recommended and the green tick that the medicine might be suitable. The Panel considered that the impression given by the table was that the risk:benefit ratio for varenicline was such that it was safer to continue to smoke than try to quit with varenicline. The Panel noted that varenicline was indicated for smoking cessation in adults and thus considered that the information given about varenicline was misleading. A breach of Clause 7.2 was ruled. The comparison of the two medicines was thus also misleading and a breach of Clause 7.3 was ruled. The implication that varenicline was not indicated as a safer alternative to smoking was not capable of substantiation and the Panel ruled a breach of Clause 7.4. The Panel considered that implying that varenicline was not indicated in smoking cessation and that continuing to smoke was safer than trying to quit with varenicline disparaged the medicine and it thus ruled a breach of Clause 8.1. The Panel noted that Clause 7.9 required that information and claims about side-effects reflect available evidence or be capable of substantiation by clinical experience. Insomuch as the table implied that it was safer to continue to smoke than take varenicline, the Panel considered that it did not reflect the available evidence regarding the risk:benefit ratio. A breach of Clause 7.9 was ruled. The Panel considered that the material did not maintain high standards and ruled a breach of Clause 9.1. All the above rulings were appealed by Johnson & Johnson.

Turning to the statement below the table that the varenicline SPC stated 'Care should be taken with patients with a history of psychiatric illness…', the Panel noted that this statement was taken from Section 4.4 of the varenicline SPC, Special warnings and precautions for use. The Panel also noted that although there were a number of warnings listed in Section 4.4 of the Nicorette Invisi 25mg Patch SPC, there was no warning in relation to use in patients with a history of psychiatric illness. In the Panel's view, it was also important to note that patients

using the Invisi Patch were already exposed to nicotine given their use of cigarettes. In that regard they had already had to manage the combined effects of nicotine and the conditions listed in Section 4.4 of the Invisi Patch SPC. The Panel did not consider that the statement about varenicline was misleading with regard to the safety profile of either medicine and ruled no breach of Clause 7.2. The statement reflected the available evidence in relation to the use of the medicines in this patient population and no breach of Clause 7.9 was ruled. The Panel noted its ruling above and ruled no breach of Clause 9.1. These rulings were not appealed.

APPEAL BY JOHNSON & JOHNSON

Johnson & Johnson submitted that the leavepiece entitled 'Designed for tolerability' was intended to provide prescribers with relevant information regarding the safety and efficacy of Nicorette Invisi 25mg Patch and the situations in which it might be appropriate to consider prescribing it.

Johnson & Johnson noted that the heading on page 4 was 'Nicorette Invisi 25mg Patch, Designed for versatility' with a subheading 'Suitable for a wide range of patient situations'. The page featured a table which compared between Nicorette Invisi 25mg Patch and varenicline in terms of key indications, cautions and contraindications. The columns in the table were headed 'Nicorette Invisipatch' and 'Varenicline', and both headings referred to the respective SPCs. Row 5 of the table ('Indicated as a Safer option to Smoking') directly compared the licensed indications for the two medicines in terms of whether they were specifically indicated as a 'safer alternative to smoking'.

Johnson & Johnson submitted that critical to this case was an understanding of the indications for the two products, and the specific wording of these indications as set out in Section 4.1 of the respective SPCs.

Johnson & Johnson submitted that when NRT was first introduced as a licensed medicine in the late 1970s it was only indicated for smokers making an immediate and complete quit attempt ie giving up smoking completely, and using NRT for a defined period in order to manage nicotine withdrawal symptoms. In 2005 a Committee on Safety of Medicines working group advised that the indication should be widened to include cutting down smoking as a 'stepping stone' to quitting completely.

Johnson & Johnson submitted that there had since been further interest in novel strategies for the use of medicinal nicotine. These strategies included temporary abstinence, where the smoker wished to avoid harming others or was unable to smoke because they were in a no-smoking environment, and harm reduction, where the smoker was not ready to quit but wished to substitute some or all of their cigarettes with medicinal NRT, with no limit on duration of use. The harm reduction strategy was outlined and endorsed in a report by the Tobacco Advisory Group of the Royal College of Physicians in 2008 which recommended that 'Use of existing [NRT] products as a temporary substitute for smoking (for example, in the home), or as a long-term substitute for smoking by those unable to quit, also needs to be encouraged'.

Johnson & Johnson submitted that the first application received by the MHRA to extend the licensed indications to include a harm reduction element for NRT was for the Nicorette Inhalator. This application was reviewed and approved by the CHM and the conclusions published in a Public Assessment Report in December 2009. In addition, the working group recommended that a harm reduction element was appropriate for inclusion within the indications of all other currently authorised forms of NRT. The wording approved by the CHM to be included within the indications of all NRT products was as follows:

'(Name of NRT…) relieves and/or prevents craving and nicotine withdrawal symptoms associated with tobacco dependence. It is indicated to aid smokers wishing to quit or reduce prior to quitting, to assist smokers who are unwilling or unable to smoke, and as a safer alternative to smoking for smokers and those around them.'

This wording had been included as part of the approved indications listed on the SPC for Nicorette Invisi 25mg Patch, however this was not an approved indication for varenicline, which was solely 'indicated for smoking cessation in adults'.

Johnson & Johnson submitted that essentially, the harm reduction indication allowed for 'open-ended' use of NRT for an undefined period, based on the premise that using NRT relieved nicotine withdrawal symptoms, and provided nicotine in a form which was safer than nicotine obtained through smoking tobacco. The expression 'Safer Option to Smoking' had been adopted to refer to this specific indication. The wording 'Indicated as a Safer Option to Smoking' which appeared in row 5 of the table was therefore a specific reference to the harm reduction indication, which was included in the approved indications for Nicorette Invisi 25mg Patch which was not an approved indication for varenicline, which was solely indicated for 'smoking cessation in adults'.

Johnson & Johnson noted that Pfizer had presented its case for six separate breaches of the Code within a single, short paragraph and that the complaints procedure was essentially an adversarial process in which the evidence to be taken into account came from the two parties and that the complainant had the burden of proving their complaint on the balance of probabilities. Given the very brief nature of Pfizer's allegations, and the lack of evidence and argument presented, Johnson & Johnson was surprised that the Panel regarded Pfizer's grounds for complaint as compelling when it had merely alleged, without any supporting argument or evidence, that the presentation of data in the table implied that the

use of varenicline was not safer than smoking. Johnson & Johnson did not believe that Pfizer had proved its complaint on the balance of probabilities.

Johnson & Johnson noted that in its ruling, the Panel agreed with Pfizer that the table implied that the risk:benefit ratio for varenicline was such that it was safer to continue to smoke rather than try to quit with varenicline. The wording of the ruling was critical. A breach of Clause 7.2 was ruled based on row 5 and 'thus the comparison of the two medicines was also misleading and a breach of Clause 7.3 was ruled.' In other words, the subsequent rulings were derived from the single, isolated consideration that row 5 implied that smoking was safer than varenicline.

Johnson & Johnson submitted that this ruling resulted from taking row 5 of the table out of context of the overall table and the additional text on the page, and that the ruling did not recognize the significant differences in approved indications between the two products. Three points were of paramount importance in considering potential breaches of the Code on this page:

1 The table directly compared certain key indications, cautions and contraindications of the two products in question, and did not compare either of the products with smoking

2 The approved therapeutic indications for Nicorette Invisi 25mg Patch were fundamentally different from varenicline

3 'Safer Option to Smoking' referred to a specific indication for Nicorette Invisi 25mg Patch which was not shared by varenicline.

Each row in the table highlighted a different aspect of Nicorette Invisi 25mg Patch and varenicline to help the prescriber make an informed decision in different patient types. These were 'Driving or operating complex machinery'; 'Hazardous activities'; 'Children or adolescents 12-18 years'; 'Pregnancy'; 'Indicated as a Safer Option to Smoking'; 'Chronic generalized dermatological disorders' and 'Hypersensitivity to the active ingredients'.

Johnson & Johnson noted that the Panel considered row 5 of the table first. Obviously, readers would not typically start at row 5 and therefore by doing so, the Panel indicated a higher prominence to this claim than would be afforded by typical readers. The Panel had therefore taken this specific comparison out of context to the remainder of the page. This challenged the overall impression of the comparisons in the table. However Johnson & Johnson also addressed the Panel's specific concerns as raised in the ruling.

Johnson & Johnson reiterated that row 5 was titled 'Indicated as a Safer Option to Smoking'. 'Indicated' clearly informed the prescriber that this referred to the approved indications as set out in Section 4.1 (Therapeutic indications) of the respective SPCs. The phrase 'Safer Option to Smoking' very closely reflected the wording in the approved indications for Nicorette Invisi 25mg Patch, which stated that the product was indicated '…as a safer alternative to smoking for smokers and those around them'; this phrase was synonymous with 'safer alternative to smoking'. Use of upper case letters in the phrase 'Safer Option to Smoking' further reinforced that this term denoted a specific indication, and that no attempt was being made to invite any more general comparison with smoking. Prescribing information on the back page included a clear description of the approved indications for Nicorette Invisi 25mg Patch, including the 'Safer alternative to smoking' indication.

Johnson & Johnson submitted that it was legitimate to compare the indications for the two products, which had a number of important differences. It was key to note that the table compared certain aspects of two products licensed for various indications to help smokers and did not make any comparisons between varenicline and smoking. The nature of the comparison was very clear, and was highlighted by the column headings ('Nicorette Invisipatch' and 'Varenicline'). It was difficult to see how prescribers could view this table as making a comparison between smoking and varenicline. Johnson & Johnson could not see how prescribers could believe the table implied that varenicline was more dangerous than smoking. Given that it was indicated for smoking cessation, and the fact that varenicline was one of the most widely prescribed medicines for smoking cessation, it was not credible that prescribers could infer that continuing to smoke was safer than attempting to quit with varenicline.

Johnson & Johnson submitted that in the context of the page heading, the subheading and the rest of the table, row 5 could only be seen as a direct, accurate and fair comparison of approved product indications, and not a comparison between varenicline and smoking. Johnson & Johnson submitted that it had never claimed directly or indirectly that varenicline was less safe than smoking in any sub-population. Johnson & Johnson had merely presented a valid and direct comparison of key indications, cautions and contraindications for Nicorette Invisi 25mg Patch and varenicline. Thus Johnson & Johnson contended that the table did not compare varenicline with an option to 'continue smoking' and did not imply that smoking was safer than taking varenicline. Johnson & Johnson appealed the ruling of a breach of Clause 7.2.

Johnson & Johnson appealed the Panel's ruling of a breach of Clause 7.3 noting that it was derived directly from the ruling of a breach of Clause 7.2 using the same overall argument about the relative safety of smoking and varenicline.

Johnson & Johnson noted that the Panel subsequently ruled a breach of Clause 7.4 because 'the implication that varenicline was not indicated as a safer alternative to smoking was not capable of substantiation'. In fact, it was a demonstrable fact that, unlike Nicorette Invisi 25mg Patch, varenicline was not specifically indicated as a safer alternative to

smoking. Therefore, Johnson & Johnson submitted that this claim was very clearly capable of substantiation, and it appealed the ruling of a breach of Clause 7.4.

Johnson & Johnson noted that the Panel further ruled a breach of Clause 8.1 for disparaging the medicine by 'implying that varenicline was not indicated in smoking cessation and that continuing to smoke was safer than trying to quit with varenicline'. Johnson & Johnson submitted that it had already made its arguments regarding the lack of positioning of varenicline against continuing to smoke and denied this interpretation. Nor could Johnson & Johnson find anything in the table that suggested that varenicline was not indicated for smoking cessation. Johnson & Johnson believed that as one of the most widely prescribed medicines for smoking cessation, prescribers would be well aware that varenicline was approved for this indication. Therefore Johnson & Johnson appealed the ruling of a breach of Clause 8.1 noting its concern that this breach was ruled partly on the grounds that the table implied varenicline was not indicated for smoking cessation, even though Pfizer had not alleged this specific point in its complaint.

Johnson & Johnson noted that the Panel then ruled a breach of Clause 7.9 for failing to represent properly the safety profile of varenicline on the grounds that the table portrayed varenicline as more dangerous than continuing smoking. The safety profile of varenicline was presented in accordance with the SPC and did not in any way imply that smoking was a safer option than taking varenicline. Johnson & Johnson therefore appealed the ruling of a breach of Clause 7.9.

Johnson & Johnson submitted that on the basis of row 5 in the table, the Panel ruled five separate breaches of the Code and then concluded that the overall presentation was such as to have breached high standards and ruled a breach of Clause 9.1. Johnson & Johnson appealed this ruling on the grounds that the five previous rulings were not valid. Even if the Appeal Board upheld some of the rulings, Johnson & Johnson did not believe that the overall presentation on this page represented a breach of high standards.

COMMENTS FROM PFIZER

Pfizer noted that Johnson & Johnson's appeal was focused on the approved indications for the two products, and the specific wording within these indications as set out in Section 4.1 of the respective SPCs. A brief history of the harm reduction campaign was also provided. Whilst this was informative, it did not justify the inappropriate portrayal and comparison of Nicorette Invisi 25mg Patch and varenicline in the table in question.

Pfizer alleged that it was not clear from the table that 'indication' had been referred to, using the regulatory definition of this word. A GP or smoking cessation specialist, for example, might not be familiar with such terminology. To state 'indicated as a safer option to smoking' could easily infer that the patch was a safer option to smoking and the opposite was so for varenicline. This was compounded by the simple 'tick' and 'cross' presentation. Johnson & Johnson argued that the comparison was only between the patch and varenicline, and not between the treatment and smoking. However, 'a safer option to smoking' invited a direct comparison on safety grounds between the treatment and smoking.

Pfizer alleged that whilst Johnson & Johnson had referred to a report by the Tobacco Advisory Group of the Royal College of Physicians in 2008 which recommended that 'Use of existing (NRT) products as a temporary substitute for smoking (for example, in the home), or as a long-term substitute for smoking by those unable to quit, also needs to be encouraged', this was substantially different to stating, with no context, 'indicated as a safer option to smoking'. Pfizer maintained that the material was unbalanced, misleading in relation to the safety of varenicline and the comparison being claimed, could not be substantiated, disparaged varenicline and did not demonstrate high standards of promotional practice. Pfizer alleged therefore that the material in question was in breach of Clauses 7.2, 7.3, 7.4, 7.9, 8.1 and 9.1.

APPEAL BOARD RULING

The Appeal Board noted the differences between the licensed indications for the two medicines. The Nicorette Invisi 25mg Patch indications included use as a safer alternative to smoking for smokers and those around them whereas varenicline was only indicated for smoking cessation in adults. The Appeal Board further noted Johnson & Johnson's submission that 'indicated' in row 5 of the table had been used in its regulatory sense. The green tick in the Invisi Patch column however, according to the key to the table meant 'may be suitable'. In the Appeal Board's view the target audience would not be familiar with the regulatory use of 'indicated' and would, given the key to the table, interpret row 5 to mean that Nicorette Invisi 25mg Patch could be used as a safer option to smoking. A red cross for varenicline would inevitably be interpreted as the opposite. The red cross in the table was stated to denote 'not recommended' and in that regard the Appeal Board noted that the phrase 'not recommended' had not been used in its regulatory sense.

The Appeal Board did not accept the submission that the table was a fair comparison of the approved product indications. The Appeal Board considered that the table suggested that varenicline was not a safer alternative to smoking as alleged and in that regard it upheld the Panel's rulings of breaches of Clauses 7.2, 7.3, 7.4, 7.9, 8.1 and 9.1. The appeal on all points was unsuccessful.

2 Page comparing NRT with varenicline

COMPLAINT

Pfizer referred to a page of the leavepiece entitled 'NRT is well tolerated and has an excellent safety profile'. Pfizer considered that use of the word 'excellent' in the description of the NRT safety profile on this page of the leavepiece and on the back page of the leavepiece was not appropriate. Nicorette Invisi 25mg Patch had adverse effects, warnings and precautions and contraindications which were listed in its SPC. Pfizer alleged that the word 'excellent' was an inappropriate adjective to use in this context, which over-claimed the safety profile of the Invisi Patch in breach of Clause 7.10.

A bar chart on the page at issue, entitled 'Adverse drug reactions in an independent study comparing NRT (all forms) and varenicline', was referenced to Stapleton *et al* (2008) and depicted a selection of 'adverse drug reactions' from the study. Pfizer stated that as there was no description of the study design, readers might assume that this was a randomised, head-to-head, clinical trial comparison between NRT and varenicline rather than an observational, non randomised, cohort study which compared a group of patients taking NRT prior to the availability of varenicline, with a different group of patients who were treated with varenicline immediately post-launch. The reporting of adverse events in these cohorts could not imply causality (the term 'adverse drug reactions' should not be used) and the reporting rate for varenicline was likely to be influenced by the proximity to launch. Pfizer did not consider it was appropriate to compare the safety information from these two distinct, non randomised, open label, observational cohorts in this way in promotional material. Furthermore, a primary objective of the study was to compare the clinical effectiveness of NRT vs varenicline in terms of quit rate. This was significantly higher in the varenicline group. Pfizer considered that fair balance would require both efficacy and safety to be shown. None of the above information was made clear on the page and hence readers were misled as to the nature and limitations of the data being presented. Pfizer alleged that the bar chart was therefore misleading and did not fully describe the design or the findings of the study. It did not allow readers to fully assess the data presented. The safety comparisons made could not be robustly substantiated by Stapleton *et al* and high standards had not been maintained, in breach of Clauses 7.2, 7.3, 7.4, 7.8, 7.9 and 9.1.

RESPONSE

Johnson & Johnson submitted the page at issue was not about Nicorette, but rather about the safety and tolerability of NRT in general compared with varenicline. The page accurately and comprehensively reflected safety data from the only published study which compared varenicline with various NRT options.

Johnson & Johnson submitted that, grammatically, 'excellent' was an adjective and not a superlative as asserted. As such it might be used as long as it could be substantiated. The company acknowledged that 'excellent' could rarely be supported when describing the safety profile of a medicine but in this case it considered it was justified and its use was accepted when Invisi Patch materials were pre-vetted by the Medicines and Healthcare products Regulatory Agency (MHRA).

Johnson & Johnson submitted that the safety profile of NRT was well established and its status as a non-prescription medicine reflected the fact that it was very well tolerated, adverse events were usually mild and transient and serious adverse drug reactions were unlikely. In fact NRT was freely available from most retail outlets without pharmacist supervision. Johnson & Johnson also noted that smokers were already routinely exposed to nicotine and were well used to 'titrating' their nicotine intake to avoid adverse effects. In addition the safety profile of nicotine was such that nicotine-containing products (such as electronic cigarettes) were available as unregulated non-medicinal products. Johnson & Johnson did not consider this would be the case if the safety profile of nicotine was not considered to be excellent.

Johnson & Johnson stated that the leavepiece was aimed at prescribers whose frame of reference was likely to be prescription medicines. It considered that in this context it was reasonable to state that the product was 'well tolerated' and had an 'excellent safety profile'. Johnson & Johnson noted that many people who quit smoking suffered from withdrawal symptoms which might often be confused with adverse events.

Johnson & Johnson submitted that NRT was used by patients who had already been using nicotine in a much more harmful format as evidenced by the statement in the Invisi Patch SPC 'Any risks that may be associated with NRT are substantially outweighed by the well established dangers of continued smoking'.

The description 'excellent' appeared above a bar chart in which the side effect profiles for NRT and varenicline were presented. These data were taken from Stapleton *et al* which directly compared varenicline with NRT and Johnson & Johnson considered provided complete context for the claim. Given this, the company did not consider the claim misleading. A direct quotation from Stapleton *et al* was also relevant as it described the side effect profile as 'benign', a term which Johnson & Johnson considered, when applied to safety, equated with 'excellent':

'Nicotine replacement therapy (NRT) has become the standard pharmacological treatment for tobacco dependence, due to its well-proven effectiveness, benign side effect profile and easy availability through pharmacy and general sales.'

Johnson & Johnson considered that smoking cessation experts would also agree that NRT had an excellent safety profile as illustrated by the following quotation from the Oxford Textbook of Primary

Medical Care: 'However, many clinicians consider NRT to be the first line drug treatment for nicotine dependence because of its excellent safety profile.'

Johnson & Johnson considered that as those who used NRT had already been exposed to nicotine, combined with the long established benign safety profile of NRT and the availability of nicotine in non-prescription medicines and even non-medicinal products, made nicotine a unique active ingredient and justified the use of 'excellent' to describe its safety profile. The company consider that the use of the word to be appropriate and that it did not breach Clause 7.10.

Johnson & Johnson considered that the data from Stapleton *et al* were reflected accurately in the bar chart and therefore not misleading. Pfizer had asserted that readers might assume this was a randomised, head-to-head clinical trial comparison as it was not specifically stated that it was an observational study. Johnson & Johnson did not consider this was necessarily the case. Many types of data were presented to prescribers including randomised studies, observational studies, case controlled studies etc. Prescribers understood this and no assertion was made that these data were from a randomised study.

Johnson & Johnson noted Pfizer's assertion that the term 'adverse drug reactions' should not be used. Johnson & Johnson submitted that it had used this term as the authors had used it as a section heading when describing these occurrences. The table from which the data were taken also described them as 'adverse drug symptoms'. The details of the assessment of these reports were not given in detail in the paper. However, Johnson & Johnson submitted that the patients were asked to report suspected adverse drug reactions and the company stated that it reflected that in its description. The authors only tabulated terms which were reported significantly more frequently in one group compared with the other.

Johnson & Johnson noted Pfizer's assertion that the safety data should not have been used from Stapleton *et al* unless efficacy data were also included in order to give a balanced comparison. Johnson & Johnson submitted that there was no requirement to provide safety and efficacy data for every clinical paper which was included in a detail aid. This page was about the safety and tolerability of NRT and there was no requirement when presenting data from a study to present data from all the outcomes considered. The efficacy of the medicines was not in question and not relevant to this particular page of the detail aid.

Johnson & Johnson considered that the bar chart was not misleading and adequately presented a clear, fair and balanced view of the data. The adverse drug reaction data were presented in full and accurately tabulated from the original paper allowing readers to fully assess of the data presented. The company considered that it was appropriate to use Stapleton *et al* to illustrate the safety profile of NRT and that these data would help a prescriber to make a prescribing decision. It did not consider that it had failed to maintain high standards and considered it had not breached Clauses 7.2, 7.3, 7.4, 7.8, 7.9 or 9.1.

PANEL RULING

The Panel noted that Pfizer had referred to two uses of the word 'excellent' to describe the safety profile of the Invisi Patch – on a page headed 'NRT is well tolerated and has an excellent safety profile' and in a bullet point on the back page. The Panel considered the two pages separately.

The heading 'NRT is well tolerated and has an excellent safety profile' was on a page which featured a bar chart adapted from Stapleton *et al*. Stapleton *et al* had compared the adverse drug reactions of varenicline (n=208) and NRT (n=204) by asking patients to report 'any unpleasant effects you think [the medicine] may have caused'. Those using NRT could choose between all licensed preparations and doses; 60% used a nicotine patch, 25% a nasal spray, 11% gum or lozenge and 5% an inhaler or microtab. The study was conducted between May 2006 and April 2007. The Nicorette Invisi 25mg Patch was first authorized in December 2008.

The Panel noted Johnson & Johnson's submission that the page at issue was about the safety and tolerability of NRT in general, and not Nicorette compared with varenicline. The Panel considered, however, that the majority of readers would assume that the results shown in the bar chart were from a comparison of the Invisi Patch with varenicline. This impression was strengthened by the claim below the bar chart 'The favourable safety and tolerability profile of Nicorette has been shown in more than 100 clinical studies'.

The Panel noted that in Stapleton *et al*, varenicline was introduced in the clinic conducting the study in January 2007 (8 months after the start of the study) after which a minority of patients chose to use NRT. Varenicline was first authorized in September 2006 and so when it was introduced in to the study it would have been a new medicine. In this regard the Panel considered that patients were more likely to report possible adverse effects with it. The bar chart showed statistically significantly greater incidences of most adverse drug reactions with varenicline than with NRT with the exception of skin irritation.

The Panel noted its concerns about the design and timing of the Stapleton study in relation to the availability of the medicines concerned. Within a Nicorette Invisi 25mg Patch leavepiece, the heading 'NRT is well tolerated and has an excellent safety profile' would be read as a claim for Nicorette Invisi 25mg Patch, supported by the Stapleton *et al* data immediately below. The Panel considered that Stapleton *et al* did not support such a claim for the Invisi Patch and in that regard the properties of the medicine had not been presented objectively. A breach of Clause 7.10 was ruled. This ruling was not appealed.

With regard to the bar chart the Panel considered that for the reasons described above in relation to Stapleton *et al* the comparisons depicted were misleading with regard to the Nicorette Invisi 25mg Patch and varenicline. Breaches of Clauses 7.2 and 7.3 were ruled. This ruling was appealed by Johnson & Johnson. The bar chart did not present data in such a way as to give a clear and balanced view of the safety profile of either product and the Panel ruled a breach of Clause 7.8. This ruling was not appealed. As Nicorette Invisi 25mg Patch was not available at the time of the Stapleton *et al* evaluation, the Panel did not consider that the incidence of side-effects presented in the bar chart were capable of substantiation in relation to Nicorette Invisi 25mg Patch, and ruled breaches of Clauses 7.4 and 7.9. This ruling was appealed by Johnson & Johnson. The Panel considered that the use of the Stapleton *et al* data in this way amounted to a failure to maintain high standards and ruled a breach of Clause 9.1. This ruling was appealed by Johnson & Johnson.

With regard to the back page of the leavepiece, this was headed 'Nicorette Invisi 25mg Patch – Designed for first line recommendation'. Under a sub-heading 'Designed for tolerability' was the bullet point 'Well tolerated with an excellent safety profile' which was referenced to Tønnesen *et al* (1999). This reported the Collaborative European Anti-Smoking Evaluation (CEASE) trial, which was a multicentre, randomized, double-blind, placebo controlled smoking cessation study comparing different doses and treatment durations of NRT. The Panel noted that the treatment used in this study was Nicorette 10mg and 15mg patches, and not the Nicorette Invisi 25mg Patch, although some patients received 25mg of nicotine by using both the 15mg and 10mg patches at the same time. Other patients received either the 15mg patch or placebo. Tønnesen *et al* noted that the overall incidence of adverse events was low and these were generally transient. Nausea/vomiting were the only reported symptoms with a higher frequency in the 25mg group (7.3%) compared with the 15mg group (5.4%); these adverse events were more common in both active treatment groups than in the placebo group (3.7%, $p<0.05$). Headache was reported in 5.6% of the 25mg group, 5.3% of the 15mg group and 3.9% of the placebo. The incidence of insomnia was 4.9%, 5.4%, and 5.9% respectively. Palpitations and tachycardia were reported by 2.25% (25mg), 2.6% (15mg) and 0.9% (placebo). Frequencies of nightmares during the first week of treatment were 8% (25mg), 7% (15mg) and 6% (placebo), compared with 7%, 8% and 7%, respectively, for the week preceding the start of treatment. The figures for vivid dreams were 20% (25mg), 18% (15mg) and 15% (placebo), compared with 18%, 19% and 17% before starting treatment. The authors stated that nightmares and vivid dreams were collected using a checklist, which they considered might explain the high frequency. Local adverse events comprised itching (25mg 14.4%, 15mg 12.9% and placebo 5%) and rash (25mg 5.2%, 15mg 5.2% and placebo 3.5%) in the patch area. Two per cent of subjects discontinued treatment due to adverse events in both the active and placebo groups. There were four myocardial infarctions during the study period which were within the expected range. The authors concluded that NRT appeared to have few side-effects.

The Panel noted the side-effects reported by Tønnesen *et al* and that night time awakenings/sleep disturbances were possible symptoms of nicotine withdrawal. The Panel also noted that from the list of six possible adverse events given in Section 4.8 of the Nicorette Invisi 25mg Patch SPC, one was very common (itching), three were common (dizziness/headache, gastrointestinal discomfort/nausea/vomiting and erythema), two were uncommon (palpitations and urticaria) and one was very rare (reversible atrial fibrillation). The SPC also stated that about 20% of Nicorette Invisi Patch users experienced mild local skin reactions during the first weeks of treatment. The SPC stated that at recommended doses the Nicorette Invisi 25mg Patch had not been found to cause any serious adverse effects. The Panel noted Johnson & Johnson's submission about the prior exposure of patients to nicotine, the long established benign safety profile of NRT and the availability of nicotine in non-prescription medicines. The Panel noted that the claim at issue appeared on the final page of the leavepiece and summarized the data within. The Panel noted its rulings above of breaches of the Code in relation to misleading safety comparisons within the leavepiece. The Panel considered that the claim was not a fair summation of the safety data within which was misleading and thus overclaimed the safety profile of Nicorette Invisi 25mg Patch as alleged. A breach of Clause 7.10 was ruled. This ruling was not appealed.

APPEAL BY JOHNSON & JOHNSON

Johnson & Johnson submitted that page 5 of the leavepiece was intended to illustrate the safety profile of all forms of NRT compared with varenicline. All forms of NRT were shown as the comparator because there were no published data directly comparing varenicline and Nicorette Invisi 25mg Patch. The page was entitled 'NRT was well tolerated and has an excellent safety profile'. Data was presented as a bar chart derived accurately and comprehensively from Stapleton *et al*. The bar chart showed the incidence of adverse reactions experienced by patients using NRT or varenicline and included the ten terms reported with a statistically significantly greater frequency in one group or the other. This page was intended to deal solely with safety and tolerability and not efficacy.

Johnson & Johnson submitted that the contested breaches on this page were ruled on a simple misinterpretation of presentation. Pfizer had alleged several breaches of the Code on page 5:

- inadequate information was provided about the study design
- the term 'adverse events' should have been used rather than 'adverse reactions'
- the study design was inherently biased
- efficacy data from the study should also have been presented for balance.

Johnson & Johnson noted that Pfizer had alleged that for these reasons, page 5 of the leavepiece was misleading and did not fully describe the design or findings of the study and did not allow readers to fully assess the data presented. Breaches of Clauses 7.2, 7.3, 7.4, 7.8, 7.9 and 9.1 were alleged.

Johnson & Johnson noted that the Panel had acknowledged the deficiencies of the study design. However, it was clear from the following extracts from the Panel's ruling that it was made upon a different basis.

'The Panel considered, however, that the majority of readers would assume that the results shown in the bar chart were from a comparison of the Invisi Patch with varenicline'

'With regard to the bar chart the Panel considered that for the reasons described above in relation to Stapleton *et al* the comparisons depicted were misleading with regard to the Nicorette Invisi 25mg Patch and varenicline'

Johnson & Johnson submitted that despite no such allegation from Pfizer, the Panel concluded that prescribers would assume that the results shown in the bar chart were from a comparison of the Nicorette Invisi 25mg Patch with varenicline. As a result the Panel ruled breaches of all six clauses. Johnson & Johnson appealed the ruling on this specific point which it was clear formed the basis of the Panel's rulings.

Johnson & Johnson submitted that a potential sources of bias existed within all studies. The possible existence of bias in a study could not therefore preclude the use of such studies in promotional material, especially where they were the best comparison available. Nor did Johnson & Johnson believe that the adverse reaction profile for varenicline demonstrated Stapleton *et al* was inherently flawed as it was generally consistent with the varenicline SPC. Apart from one prospective study with a patch which was neither manufactured by Johnson & Johnson nor the same strength as the Nicorette Invisi Patch, Stapleton *et al* was the only study which compared the safety profile of any NRT product with varenicline. Furthermore, prescribers would value an insight into the safety profiles of NRT and varenicline which had been gathered from a study of routine therapeutic use.

In hindsight Johnson & Johnson acknowledged that the bar chart would have presented a more complete picture if it had been accompanied by further information on the study design and methodology and so it had accepted the ruling of a breach of Clause 7.8. However it did not see how it could have been made clearer that the bar chart represented NRT rather than Nicorette Invisi Patch, and it contended that it was valid and helpful for the prescriber to provide data from a comparison with all forms of a chemical entity where no comparison was available with a specific formulation.

Johnson & Johnson submitted that it was clearly stated three times on page 5 that the data related to NRT in general rather than any specific form or brand. The page heading clearly indicated that this was a depiction of the tolerability of NRT overall. The bar chart featured on the page was clearly headed 'Adverse drug reactions in an independent study comparing NRT (all forms) and varenicline.' In addition, the key to the bar chart stated 'NRT (n=204)'. In contrast to the other pages within the leavepiece, there was no mention in the page heading or anywhere else on the page of the specific product Nicorette Invisi Patch. The word Nicorette appeared once, below the bar chart in a separate claim and the use of the Nicorette brand name rather than the Nicorette Invisi 25mg Patch product name clearly indicated that this was a brand and not a formulation-specific claim.

Johnson & Johnson submitted that it was therefore abundantly clear that the intention of the page and the chart was to consider the safety profile of NRT in general, rather than any specific form and/or brand of NRT. In its complaint, Pfizer acknowledged that the reader would assume this was a comparison between NRT and varenicline, and Pfizer alleged that prescribers would assume that the bar chart compared Nicorette Invisi Patch with varenicline. Johnson & Johnson again noted that the burden of proof rested with the complainant, and that the evidence taken into account should come from the complainant and the respondent. However, in this case the Panel had ruled multiple breaches on a pivotal argument that was never presented by Pfizer.

Johnson & Johnson submitted that it was important to note that the target audience was very familiar with the various forms of NRT and the various formulations of Nicorette specifically. It was highly unlikely that a typical prescriber would conclude, as the Panel had done, that the bar chart presented Nicorette Invisi 25mg Patch data specifically.

The Panel's interpretation that the bar chart portrayed Nicorette Invisi 25mg Patch specifically had led to several rulings of breaches of the Code which Johnson & Johnson submitted were unreasonable and incorrect.

Johnson & Johnson noted that the Panel ruled breaches of Clauses 7.2 and 7.3 in that the bar chart misrepresented a comparison between Nicorette Invisi 25mg Patch and varenicline. Johnson & Johnson appealed these rulings. The product name 'Invisi 25mg Patch' did not appear anywhere on the page, and three separate references to 'NRT' made it clear to the prescriber that the data presented referred to NRT in general.

Johnson & Johnson submitted that on the basis that the Nicorette Invisi 25mg Patch was not launched at the time of Stapleton *et al*, the Panel ruled breaches of Clause 7.4 in that the study failed to substantiate the claims for Nicorette Invisi 25mg Patch and of Clause 7.9 in that it misrepresented the safety profile of Nicorette Invisi 25mg Patch. Johnson & Johnson

submitted that as stated above, there was no specific reference to Nicorette Invisi 25mg Patch on the page in question which depicted all forms of NRT. Therefore Johnson & Johnson could not see how it could be held in breach for either clause. The bar chart accurately depicted the data presented in Stapleton *et al* and was therefore capable of substantiation. No attempt had been made on the page to present safety information on Nicorette Invisi 25mg Patch, and so the safety profile of Nicorette Invisi 25mg Patch could not possibly have been misrepresented.

Johnson & Johnson submitted that the combined interpretation of the rulings was such that the Panel then considered that high standards had not been maintained and ruled a breach of Clause 9.1. Johnson & Johnson appealed this ruling on the grounds that the Panel had misunderstood the data presented in a way that a typical prescriber would not.

COMMENTS FROM PFIZER

Pfizer noted that Stapleton *et al* was an observational, non-randomised, cohort study which compared a group of patients taking NRT prior to the availability of varenicline, with a different group of patients who were treated with varenicline immediately post-launch. A breach of Clause 7.8 had been accepted by Johnson & Johnson as it acknowledged in hindsight that the bar chart would have presented a more complete picture if it had been accompanied by further information on the study design and methodology. In addition Johnson & Johnson had accepted breaches of Clause 7.10 through over-stating the safety profile of Nicorette Invisi 25mg Patch.

Pfizer considered, therefore, that it seemed that Johnson & Johnson had accepted two fundamental issues with this material. Pfizer alleged that as the exact nature of the data shown was not made clear to the reader the bar chart was misleading in breach of Clauses 7.2 and 7.3. It did not allow the reader to be fully informed about the data to make an evaluation of the medicines or a comparison of the medicines. Stapleton *et al* was not sufficiently robust to be able to make safety comparisons and claims between NRT (or Nicorette Invisi 25mg Patch) and varenicline because of the design limitations. Pfizer alleged that the safety comparisons could not be substantiated in breach of Clauses 7.4 and 7.9.

Pfizer alleged that taken together, high standards had not been demonstrated (in breach of Clause 9.1) by using this data to make safety and tolerability claims, which appeared to be the main purpose of the leavepiece which had the overarching claim on page 1 of 'Designed for Tolerability.' Pfizer alleged that page 5 of the leavepiece was in breach of Clauses 7.2, 7.3, 7.4, 7.9 and 9.1.

APPEAL BOARD RULING

The Appeal Board noted that the title of the bar chart referred to 'Adverse drug reactions'. Although this term was also used in Stapleton *et al*, the correct regulatory term was 'adverse drug events'.

The Appeal Board noted that Stapleton *et al* was an efficacy study and more patients gave up smoking with varenicline compared with NRT. In the Appeal Board's view many of the adverse events listed could have been symptoms of nicotine withdrawal and not adverse drug events *per se*. In that regard patients on varenicline would be expected to have a higher incidence of such symptoms than those taking NRT.

The Appeal Board noted Johnson & Johnson's submission that the page at issue was about the safety and tolerability of NRT in general, and not Nicorette compared with varenicline. However, the Appeal Board considered that in a Nicorette Invisi Patch leavepiece, which on a previous page had compared Nicorette Invisi Patch with varenicline, readers would assume 'NRT (all forms)' to have at the very least included data for Nicorette Invisi 25mg Patch which was not so. Nicorette Invisi 25mg Patch was not available over the time period covered by Stapleton *et al*.

The Appeal Board considered that the majority of readers would assume that the results shown in the bar chart were from a comparison of the Nicorette Invisi 25mg Patch with varenicline and this impression was strengthened by the claim below about Nicorette.

The Appeal Board considered that in relation to Stapleton *et al* the bar chart depicted a misleading comparison between Nicorette Invisi Patch and varenicline. The Appeal Board did not consider that the incidence of adverse events presented in the bar chart were capable of substantiation in relation to Nicorette Invisi Patch; high standards had not been maintained. The Appeal Board upheld the Panel's rulings of breaches of Clauses 7.2, 7.3, 7.4, 7.9 and 9.1. The appeal on all points was unsuccessful.

Complaint received **31 January 2012**

Case completed **21 June 2012**

NOVO NORDISK v BRISTOL-MYERS SQUIBB and ASTRAZENECA

Arrangements for a symposium

Novo Nordisk alleged that a symposium, 'The Kidney in Type 2 Diabetes: Victim or Target?' which was jointly sponsored by Bristol-Myers Squibb and AstraZeneca, promoted dapagliflozin (an SGLT-2 [sodium–glucose transporter-2] inhibitor) before the grant of a marketing authorization. The symposium took place at the Primary Care Diabetes Society (PCDS) conference. In particular, Novo Nordisk alleged that the attendance at the symposium of representatives from Bristol-Myers Squibb implied that the event was promotional. Novo Nordisk submitted that allowing the representatives to be there demonstrated that the sponsors did not intend to control who attended.

Novo Nordisk submitted that it had been given a summary of the topics discussed but without a copy of the slides, which the sponsors had refused to provide, it was difficult to know whether the symposium was fair and balanced or whether there was undue emphasis on dapagliflozin.

Novo Nordisk noted that it had similarly not been given a copy of the speakers' briefs and although an extract had been provided which referred to an 'educational meeting' and 'fair and balanced interpretation and analysis of the data' it was difficult to know if the speakers had been adequately briefed on a topic where pre-licence data was to be discussed.

Novo Nordisk considered that as the approval of a marketing authorization for dapagliflozin was imminent then it was more difficult to argue that the symposium was the legitimate exchange of medical and scientific information and not promotion.

The detailed response from Bristol-Myers Squibb on behalf of both companies is given below.

The Panel noted Bristol-Myers Squibb and AstraZeneca's submission that the annual national PCDS meeting was a legitimate site for appropriate scientific exchange. Supplementary information to the Code 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. The Panel noted that it had been alleged that dapagliflozin, an unlicensed medicine, had been promoted at the symposium. That the symposium might elicit interest in the medicines discussed was not necessarily unacceptable if the arrangements for the symposium and its content complied with the Code.

The Panel noted that a complainant had the burden of proving the complaint on the balance of probabilities.

With regard to the alleged presence of the sponsors' sales representatives at the symposium, the Panel noted a difference of opinion. Bristol-Myers Squibb was clear that neither its nor AstraZeneca's representatives had attended. Briefing material clearly stated, *et al*, that the sales team could not attend.

The Panel considered that there was no evidence to show that the sponsors' representatives attended the meeting; conversely the briefing material clearly showed that they were instructed not to attend. The Panel ruled no breach of the Code. The fact that there was not a list of attendees did not in itself mean the meeting was promotional and on this narrow point no breach of the Code was ruled.

The Panel noted that the Chairman and both speakers at the symposium were independent health professionals. The first presentation discussed, *et al*, currently available medicines. The title slide of the second presentation clearly stated 'This presentation contains information relating to drugs which are in clinical development and do not have marketing authorisation'. The first 4 slides referred to the kidney's role in hyperglycaemia. The next slide referred to SGLT-2 inhibition and its effect in reducing renal glucose reabsorption. Details of the developmental phase of five SGLT-2 inhibitors were provided; four in phase 3 development and the fifth was described as phase 2/3. The next 4 slides showed phase 2 data for canagliflozin. This was followed by 6 slides detailing the design and outcome of a phase 3 double-blind study for dapagliflozin vs glipizide in patients taking open-label metformin. The Panel noted that the style of the slides was low key and scientific. Dapagliflozin was not emboldened and there was no use of a product or company logo. The only reference to SGLT-2 inhibitors on the summary slide was the statement 'SGLT-2 inhibitors are in clinical development'.

The Panel was concerned about a number of aspects particularly the amount of data presented and the nature of that data albeit this was the only clinical data available at the time. The Panel did not accept Bristol-Myers Squibb and AstraZeneca's submission that there was no focus on any of the medicines in development. Phase 2 outcome data had been given for one of the medicines, no data for three others and positive phase 3 data for the Bristol-Myers

Squibb/AstraZeneca product which was expected to receive its marketing authorization later in 2012.

The overall meeting objectives were: to provide a non-promotional forum for scientific and medical exchange on the kidney both as an organ affected during type 2 diabetes and as a potential target in the management of type 2 diabetes; to discuss the various glycaemic treatment options for type 2 diabetes patients with chronic kidney disease (stages 3 - 5) and to explore emerging anti-diabetes therapies that target the kidney for the management of type 2 diabetes. The speaker briefs included suggested topics to be covered and stated that they could provide input to shape their presentation as deemed appropriate. The speakers were requested to provide their slides for examination by Bristol-Myers Squibb and AstraZeneca. The speakers' briefs mentioned the need to highlight any discussion that was off licence or not licensed but there was no advice that promotion of an unlicensed indication or medicine would be a breach of the Code. The suggested topics for the first speaker included issues with current treatment options in certain patients and what did newer agents offer. Similarly the second speaker was asked to cover current unmet needs in the management of type 2 diabetes and molecules in development that targeted the kidneys.

The Panel noted that some of the comments provided as feedback on the symposium referred favourably to the level of interaction and discussion.

The Panel reviewed the DVD of the symposium and noted that one speaker stated that dapagliflozin was 'probably going to be the first of this class of agents [SGLT-2 inhibitors] to hit the market' although no further details were given.

The Panel noted its comments above; its main concern was whether the arrangements met the requirements for the legitimate exchange of medical and scientific information. The event was held in November 2011, at least 7 months before the marketing authorization for dapagliflozin was expected.

The Panel considered that Novo Nordisk had not, on the balance of probabilities, proven its complaint that the symposium promoted an unlicensed medicine. Thus the Panel ruled no breach of the Code including no breach of Clause 2.

Novo Nordisk Limited complained about a symposium jointly sponsored by Bristol-Myers Squibb Pharmaceuticals Limited and AstraZeneca UK Limited, entitled 'The Kidney in Type 2 Diabetes: Victim or Target?', which took place at the Primary Care Diabetes Society (PCDS) conference in November 2011. The flyer for the symposium clearly stated 'This is a medical education symposium organised and funded by Bristol-Myers Squibb and AstraZeneca'. Novo Nordisk alleged that the symposium promoted dapagliflozin (a SGLT-2 [sodium-glucose transporter-2] inhibitor), which had yet to receive a marketing authorization, in breach of Clauses 3, 9.1 and 2 of the Code.

COMPLAINT

Novo Nordisk submitted that several sales representatives from Bristol-Myers Squibb were present at the event which implied that the symposium was promotional. During inter-company dialogue, Bristol-Myers Squibb and AstraZeneca denied that any sales representatives attended. Novo Nordisk stated that it twice requested a copy of the representatives' briefing document but this was not provided by Bristol-Myers Squibb or AstraZeneca. The companies instead confirmed the existence of a briefing document and provided the following quotation from it: 'the sales team cannot attend the symposium, should not proactively invite HCPs [health professionals] to the symposium and should not access or distribute material relating to the symposium'. Novo Nordisk considered that without seeing the entire content of this briefing document, it was difficult to assess whether the instructions provided to the representatives were adequate.

Novo Nordisk stated that a member of its sales force had seen representatives from Bristol-Myers Squibb at the symposium which indicated that there was no intention by Bristol-Myers Squibb and AstraZeneca to control who could enter the symposium. In Novo Nordisk's view, a medical educational event should have a proper registration process with personalised invitations sent out beforehand to ensure that only a relevant audience could enter.

During inter-company dialogue, Bristol-Myers Squibb gave Novo Nordisk a summary of the topics that were discussed during the symposium, but Bristol-Myers Squibb and AstraZeneca had refused to provide copies of the slides presented. Without this information Novo Nordisk considered it difficult to gain a clear understanding as to whether the content of the symposium was fair and balanced and provided focus on all SGLT-2 inhibitors in development, or whether there was an undue emphasis placed on dapagliflozin.

Novo Nordisk submitted that Bristol-Myers Squibb and AstraZeneca had also refused to provide copies of the speaker briefing documents and had only provided the following quotation from them: 'the meeting is non-promotional and the aim is to provide an educational meeting that will facilitate the exchange of scientific and medical information, which the audience may find interesting and relevant. It is also hoped that this meeting will enhance the current state of scientific knowledge and we ask that speakers give a fair and balanced interpretation and analysis of data, describing competitor products where applicable'. Novo Nordisk submitted that without viewing the speaker briefing document in its entirety it was challenging to appreciate whether the speakers were briefed adequately on a topic where pre-licence data regarding a medicine was to be discussed.

Novo Nordisk was aware that the approval of a marketing authorization for dapagliflozin was imminent. Bristol-Myers Squibb had submitted

during inter-company dialogue that 'in the context of scientific exchange, information on drugs in development can be discussed legitimately, and timing of launch should bear no relevance on this…'. Novo Nordisk considered that the closer the granting of a marketing authorization, the more difficult it was to argue that activities such as this symposium were the legitimate exchange of medical and scientific information and not promotion. The Panel highlighted this point with Novo Nordisk in Case AUTH/2234/05/09.

In summary, without being able to review all the evidence surrounding the arrangements for the symposium, Novo Nordisk was concerned that the event promoted a product prior to the grant of a marketing authorization.

RESPONSE

Bristol-Myers Squibb responded on behalf of both companies.

Bristol-Myers Squibb and AstraZeneca were concerned that because Novo Nordisk had not presented any objective evidence to them in its initial inter-company dialogue, and no evidence to the Authority in its subsequent formal complaint, they were being asked to defend unclear and unsubstantiated allegations. While a complaint might be raised if information was put forward which suggested the Code might have been contravened, the burden of proving the complaint, on the balance of probabilities, rested with the complainant and not the respondent. Given that no such evidence was presented by Novo Nordisk during inter-company dialogue, it was impossible for the companies to either defend, accept or concede any point raised in the complaint.

Bristol-Myers Squibb and AstraZeneca submitted that no member of either sales force was present at this medically-led and organised satellite symposium. Novo Nordisk had provided no evidence to support its allegation and Bristol-Myers Squibb and AstraZeneca were able to provide evidence to the contrary. All sales force who were present at the wider PCDS meeting were explicitly briefed in writing not to attend the symposium (copy provided). An on-site verbal briefing to the same effect was also delivered by the medical team. Neither was either sales force involved in the invitation process – the only invitation was solely distributed via a 'bag drop', ie in the delegate bags of registered attendees of the PCDS conference.

Bristol-Myers Squibb and AstraZeneca submitted that the Code did not require a proper registration process for a medical educational event with personalised invitations sent out beforehand to ensure that only a relevant audience could enter. Indeed, the approach suggested by Novo Nordisk seemed more appropriate to a specifically tailored and targeted commercial meeting, as opposed to the open, transparent and legitimate exchange of scientific information as permitted and outlined in the Code.

Membership of the PCDS was only open to health professionals working in primary care and it focused on those with a specialist interest in diabetes. The society aimed 'to support primary care professionals to deliver high quality clinically effective care, in order to improve the lives of people living with diabetes'. Bristol-Myers Squibb and AstraZeneca had taken the view, with reference and aligned to Case AUTH/2310/4/10, that this was an appropriate setting for such exchange of scientific information.

Bristol-Myers Squibb and AstraZeneca stated that the vast majority of diabetics were managed day-to-day in primary care, with members of the PCDS taking an active and leading role. This was reflected in the breakdown of attendees at the congress: GPs 35%, GPs with special interest 3%, diabetes specialist nurses 21%, practice nurses 24% and consultants or specialist registrars 2%. Novo Nordisk had agreed during inter-company dialogue that the annual national PCDS meeting was a legitimate site for appropriate scientific exchange.

Bristol-Myers Squibb and AstraZeneca submitted that the topic chosen was broad and clinically relevant to the PCDS attendees. The invitation was in the delegate bag which attendees received on their arrival and registration at the conference. The satellite symposium followed a keynote lecture and a clear announcement was made about the start of a sponsored satellite symposium. At that point, around half of the audience left, leaving only those interested in the symposium topic. Bristol-Myers Squibb and AstraZeneca therefore considered that the symposium was relevant to the audience and that there was no real risk of accidental attendance at the meeting by members of the public or others who were not health professionals.

Bristol-Myers Squibb and AstraZeneca considered that this approach was open, transparent, non-promotional and therefore appropriate in the context of the PCDS national conference. Pursuing the Novo Nordisk approach of a closed satellite symposium with a targeted, profiled and proactive approach would be against the spirit of such open, transparent and legitimate scientific exchange. It seemed to Bristol-Myers Squibb and AstraZeneca that the use of personalised invitations could imply that individuals had been specifically targeted and selected according to some hidden agenda.

Bristol-Myers Squibb and AstraZeneca explained that the symposium at issue examined the effect of diabetes on the kidney and the effect of the kidney on diabetes, and explored possible therapeutic options. The topic for the symposium was chosen to be relevant to an audience at the forefront of diabetes management. Chronic kidney disease (CKD) affected almost a third of all type 2 diabetics in the UK and was likely to be an eventual complication in most patients given the progressive nature of the disease. These patients could be challenging to manage given the limited treatment options available and the high risk of complications. There was also a growing body of evidence of the role of the kidney in compounding hyperglycaemia,

contributing to the so called 'ominous octet' of pathophysiologies of type 2 diabetes.

Bristol-Myers Squibb and AstraZeneca submitted that the first half of the slide deck was about the relationship of diabetes and CKD; the second half was about the effect of the kidney on glucose reabsorption. Copies of the slides were provided. Bristol-Myers Squibb and AstraZeneca stated that the 'ominous octet' of pathologies was explained by the second speaker at the symposium who detailed the role of the various organs in contributing to hyperglycaemia. The physiology of renal handling of glucose was then explored. Finally, the possibility of using the kidney as a therapeutic target was addressed. The unlicensed and exploratory nature of these medicines was made clear at the start of the presentation, both verbally and on the slides. The class of medicines explored was the SGLT-2 inhibitors. All current compounds in phase 3 development were shown (canagliflozin, dapagliflozin, empagliflozin, ipragliflozin and tofogliflozin).

Bristol-Myers Squibb and AstraZeneca submitted that the only compounds that had clinical data available at the time of the presentation were canagliflozin and dapagliflozin, both of which were in phase 3 development. Only dapagliflozin had reported phase 3 data at the time of the symposium. A fair and accurate balance was addressed by presenting the most contemporaneous data from the latest international diabetes conferences (American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD)) and in the spirit of legitimate scientific exchange.

Bristol-Myers Squibb and AstraZeneca stated that of the 40 slides presented, one referred to all SGLT-2 inhibitors and their current phase of development. Six slides (one trial design, two efficacy and three safety slides) discussed dapagliflozin, while four slides discussed canagliflozin. There was no focus on any of the medicines in development; any discussion of dapagliflozin was therefore appropriate in the context of an accurate and balanced scientific discussion of such future therapies.

Bristol-Myers Squibb and AstraZeneca considered that the discussion of the relevant topic was fair, accurate, balanced and non-promotional. The audience was appropriate as was the amount of time spent on molecules under development proportionate to the pathophysiology of diabetes, based on the latest available information. Finally, the agenda allowed time for a proper question and answer session, to facilitate scientific exchange. This was a very animated session, with the majority of questions about the management of CKD in type 2 diabetics. The audience even elected to extend the question and answer session by ten minutes which further emphasised the educational nature of the event. Independent feedback collected by the congress organizers voted the symposium very highly with a score of 91%, the highest of all the symposia at the PCDS conference.

Bristol-Myers Squibb and AstraZeneca did not have a copy of the summary of product characteristics (SPC) for dapagliflozin and the marketing authorization application was filed with European Medicines Agency (EMA) in December 2010.

Bristol-Myers Squibb and AstraZeneca considered that the symposium was conducted within the spirit of legitimate exchange of medical and scientific information and to the letter of the Code, with no disguised or pre-licence promotion of dapagliflozin, either intentionally or inadvertently. The symposium was organized, funded and developed by the medical team, with no involvement of the marketing or sales teams from either company. The topic chosen was broad, appropriate and highly relevant to those registered to attend the PCDS conference; they were dedicated to managing patients with diabetes and had a genuine interest in relevant medicines in clinical development.

Bristol-Myers Squibb and AstraZeneca submitted that the chair and speakers were carefully briefed to deliver non-promotional, fair, balanced, up-to-date and clinically relevant presentations for the symposium with the intention of enhancing scientific knowledge of the audience. There should be an unbiased view of the topics discussed. Copies of the speaker briefs were provided.

To keep true with the spirit of scientific exchange and Code requirements, speakers were asked to ensure all data presented was accurate, balanced, fair, objective, unambiguous, based on an up-to-date evaluation of all the evidence, not misleading, capable of substantiation and not disparaging or disrespectful to competitor companies or products.

To ensure that the presentations were non-promotional, speakers were asked to use non-proprietary names where appropriate and not to present product logos and to highlight both verbally and with a statement on the slides if products referred to were discussed in an off-licence manner or were not yet licensed.

Bristol-Myers Squibb and AstraZeneca reiterated their view that this was a high quality and fully compliant, non-promotional educational meeting to support the legitimate exchange of scientific information. The companies therefore refuted the alleged breaches of Clauses 2, 3 and 9.1.

Bristol-Myers Squibb and AstraZeneca submitted that throughout this matter they had complied with the spirit and letter of the Code; the symposium in question was conducted to the highest standards, in line with the Code, and they had been fully transparent and forthright with the Panel to demonstrate this.

Following a request for further information, Bristol-Myers Squibb and AstraZeneca submitted that the marketing authorization application for dapagliflozin was filed with the EMA in December 2010. An opinion from the Committee for Human Medicinal Products (CHMP) was expected in the second quarter

2012, with a decision on marketing authorization expected approximately two months later. Assuming that there were no further steps or aspects to be addressed, the earliest that the marketing authorization was anticipated was the third quarter of 2012.

Bristol-Myers Squibb stated that it had filmed the symposium for potential internal use only (a DVD copy was provided). There were no specific plans to use this material; to date it had not been used in any way either internally or externally.

In summary Bristol-Myers Squibb and AstraZeneca stated that the symposium lasted 62 minutes with the majority of time spent discussing a relevant disease area, pertinent to the audience, allowing almost 25% of the time for discussion and feedback; only a small fraction of time was spent discussing specific medicines. Any discussion clearly signposted these as being unlicensed and this was reinforced verbally on three occasions by the speakers. Of the 10 minutes spent discussing developmental SGLT-2 inhibitors, 3 minutes were spent on the canagliflozin phase 2 data and 7 minutes on the dapagliflozin phase 3 data, reflecting the latest publicly available data at the time of the presentation.

The speaker slides were not made available to the delegates of the symposium although health professionals could request copies through medical information. The potential to provide the slides in this way was not raised or highlighted, either as part of the meeting or in any other materials relating to the meeting. To date, no requests for these slides had been received.

The symposium booklet was given to all delegates of the symposium to aid note taking. The companies did not envisage that there would be any requests for the booklet following the symposium and to date, no requests for copies had been received.

PANEL RULING

The Panel noted Bristol-Myers Squibb and AstraZeneca's submission that the annual national PCDS meeting was a legitimate site for appropriate scientific exchange. 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 Clause 3 or any other clause. The Panel noted that it had been alleged that dapagliflozin, an as yet unlicensed medicine, had been promoted at the symposium. That the symposium might elicit interest in the medicines discussed was not necessarily unacceptable if the arrangements for the symposium and its content satisfied the supplementary information to Clause 3.1.

The Panel considered that when determining whether a meeting promoted a medicine before the grant of a marketing authorization, or was the legitimate exchange of medical and scientific information, the content and context in which it took place were important as were the general arrangements.

The Panel noted that the symposium had taken place in the context of the PCDS conference. In that regard the Panel considered that such conferences might be an appropriate setting for the legitimate exchange of medical and scientific information. The Panel did not consider, however, that symposia which took place in association with learned society conferences would automatically be regarded as the legitimate exchange of medical and scientific information.

The Panel noted that a complainant had the burden of proving the complaint on the balance of probabilities.

With regard to the alleged presence of Bristol-Myers Squibb and AstraZeneca sales representatives at the satellite symposium, the Panel noted that there was a difference of opinion. One of the Novo Nordisk representatives who had attended the symposium reported seeing sales representatives from Bristol-Myers Squibb at the event. Bristol-Myers Squibb was clear that neither its nor AstraZeneca's representatives had attended the satellite symposium. With regard to the symposium at issue the briefing material clearly stated that the sales team could not attend, it should not proactively invite health professionals and if information was discussed it should refer health professionals to the medical team or to the communications agency for a symposium flyer. The briefing material referred to the symposium flyers as invitations. These would be included in the delegate packs and were not to be distributed from the disease education stands. Symposium booklets would be made available to the delegates during the symposium. The sales team should not access or distribute any material relating to the symposium.

The Panel noted that Bristol-Myers Squibb and AstraZeneca did not know which of the PCDS delegates attended the satellite symposium. There was no requirement in the Code for it to do so. However, for companies to claim that symposia were the legitimate exchange of medical and scientific information the status of the audience was relevant; delegates should be able to participate in debate for it to be an exchange of medical and scientific information.

The Panel considered that there was no evidence to show that Bristol-Myers Squibb or AstraZeneca sales representatives attended the meeting; conversely the briefing material clearly showed that they were instructed not to attend. The Panel ruled no breach of Clauses 9.1, 3.1 and 2 in this regard. Similarly, the fact that there was not a list of attendees did not in itself mean the meeting was promotional. Thus on this narrow point no breach of Clauses 9.1, 3.1 and 2 was ruled.

The Panel noted that the Chairman and both speakers at the symposium were independent health professionals. The meeting agenda detailed in the speaker briefing documents showed that after a 5 minute introduction there were two 15 minute presentations, 'Renal impairment and type 2 diabetes' and 'Can the kidney provide a new solution to old problems?' This was followed by ten minutes of questions and answers. The meeting was scheduled to last 45 minutes. In total 40 slides were presented. The first presentation discussed, *et al*, currently available medicines. The title slide of the second presentation clearly stated 'This presentation contains information relating to drugs which are in clinical development and do not have marketing authorisation'. The first 4 slides referred to the kidney's role in hyperglycaemia. The next slide referred to SGLT-2 inhibition and its effect in reducing renal glucose reabsorption. Details of the developmental phase of five SGLT-2 inhibitors were provided; four in phase 3 development and the fifth was described as phase 2/3. The next 4 slides showed phase 2 data for canagliflozin. This was followed by 6 slides detailing the design and outcome of a phase 3 double-blind study for dapagliflozin vs glipizide in patients taking open-label metformin. Results were shown for HbA1c, weight, hypoglycaemia and adverse events over two years. The Panel noted that the style of the slides was low key and scientific. Dapagliflozin was not emboldened and there was no use of a product or company logo. The only reference to SGLT-2 inhibitors on the summary slide was the statement 'SGLT-2 inhibitors are in clinical development'.

The Panel was concerned about a number of aspects particularly the amount of data presented and the nature of that data albeit this was the only clinical data available at the time. The Panel did not accept Bristol-Myers Squibb and AstraZeneca's submission that there was no focus on any of the medicines in development. Phase 2 outcome data had been given for one of the medicines, no data for three others and positive phase 3 data for the Bristol-Myers Squibb/ AstraZeneca product which was expected to receive its marketing authorization later in 2012.

The overall meeting objectives according to the Chairman's brief were threefold: to provide a non-promotional forum for scientific and medical exchange on the kidney both as an organ affected during type 2 diabetes and as a potential target in the management of type 2 diabetes; to discuss the various glycaemic treatment options for type 2 diabetes patients with chronic kidney disease (stages 3 - 5) and to explore emerging anti-diabetes therapies that target the kidney for the management of type 2 diabetes.

The speaker briefs included suggested topics to be covered and stated 'The scope of your presentation is in italics and we are happy for you to provide input to shape your presentation as deemed appropriate'. The speakers were requested to provide their slides for examination by Bristol-Myers Squibb and AstraZeneca.

The speakers' brief referred to the meeting as non-promotional with the aim being to provide an educational meeting that would facilitate the exchange of scientific and medical information. There was mention of the need to highlight any discussion that was off licence or not licensed. Further the speaker brief stated 'It is also hoped that this meeting will enhance the current state of scientific knowledge and we ask that speakers give a fair and balanced interpretation and analysis of data, describing competitor products where applicable'. There was no advice that promotion of an unlicensed indication or medicine would be a breach of the Code.

The six suggested topics for the first speaker included issues with current treatment options in certain patients and what newer agents offered. Similarly the second speaker was asked to speak about current unmet needs in the management of type 2 diabetes and molecules in development that targeted the kidneys.

The Panel noted that some of the comments provided as feedback on the symposium referred to the interesting information on new medicines; other comments were complimentary about the speakers and some delegates referred favourably to the level of interaction and discussion.

The symposium booklet gave the CVs of the speakers and reproduced four of each speakers' slides. None of these slides referred to any medicine.

The Panel reviewed the DVD of the symposium and noted that the second speaker, when presenting data on dapagliflozin, stated that the medicine was 'probably going to be the first of this class of agents [SGLT-2 inhibitors] to hit the market' although no further details were given.

The Panel noted all its comments above. Its main concern was whether the arrangements met the requirements for the legitimate exchange of medical and scientific information. The event was held in November 2011 and the earliest that the marketing authorization was expected was the third quarter of 2012, ie at least 7 months after the symposium had taken place.

The Panel considered that Novo Nordisk had not, on the balance of probabilities, proven its complaint that the symposium promoted an unlicensed medicine. Thus the Panel ruled no breach of Clause 3.1 of the Code and consequently no breach of Clauses 9.1 and 2.

Complaint received **8 February 2012**

Case completed **28 May 2012**

CASE AUTH/2481/2/12

MUSLIM AFFAIRS SPECIALIST v PROSTRAKAN

Promotion of Adcal-D_3 Caplets

An NHS and Muslim affairs advisor to a healthcare management company complained that ProStrakan representatives had described Adcal-D_3 Caplets (calcium carbonate and vitamin D3) as Halal without the necessary approval from a relevant Halal certifying body. The complainant noted the conduct of one local representative in that regard.

The detailed response from ProStrakan is given below.

The Panel noted ProStrakan's submission that the gelatin free status of the new caplets used in Adcal-D_3 together with the fact that the vitamin D in the medicine was derived from a Halal source might have led to the misconception that the caplets were Halal.

The Panel noted ProStrakan's submission that no promotional material for Adcal-D_3 Caplets contained a claim about the suitability of the medicine for Halal diets and that promotion of the medicine as a Halal option was never its aim or intention. Most of the promotional material provided referred to the fact that Adcal-D_3 Caplets were gelatin free; none of it referred to the medicine being suitable for those following a Halal diet. The Panel noted however that representatives' briefing material contained the statement that 'A key feature which will appeal to many patients is that Adcal-D_3 Caplets are gelatin free, and therefore suitable for vegetarians, and patients adhering to strict halal diets'.

In the Panel's view, although the caplets were gelatin free and the vitamin D was derived from a Halal source, Adcal-D_3 Caplets as a product were not Halal. The Panel considered that the claim in the briefing document that Adcal-D_3 Caplets were suitable for patients adhering to strict Halal diets was misleading and could not be substantiated. Breaches of the Code were ruled. The briefing material advocated a course of action that was likely to lead to a breach of the Code and in that regard the company had failed to maintain high standards. Further breaches of the Code were ruled. These rulings were upheld on appeal.

With regard the activity of the representative in question, the Panel noted that the parties' accounts differed. The complainant had referred to second and third hand reports that the representative had discussed the Halal status of Adcal-D_3 Caplets. No details of the discussions were provided. ProStrakan submitted that the representative had stated that he had never claimed that the caplet itself was Halal; the term Halal had been discussed but only in response to customer questions about the source of the vitamin D. However, the representatives' briefing material stated that Adcal-D_3 Caplets were suitable for patients on a strict Halal diet and so in that regard the Panel considered that on the balance of probabilities the representative had implied that the medicine had been granted Halal status. Although the representative had used material provided by the company and followed company instructions all the relevant requirements of the Code had not been complied with. A breach of the Code was ruled.

Upon appeal, the Appeal Board noted the statement 'A key feature which will appeal to many patients is that Adcal-D_3 Caplets are gelatin free, and therefore suitable for vegetarians, and patients adhering to strict halal diets' in the representatives' briefing material dated August 2011. The Appeal Board noted from ProStrakan that this statement had been included to equip representatives with a means to respond to questions from health professionals; the company did not expect the representatives to use the claim promotionally. The Appeal Board considered, however, that briefing material was part of the promotional material for the product and describing something as a 'key feature' would have highlighted its importance as a point to note.

The Appeal Board considered that the representative who had used the briefing document to refer to the Halal status of Adcal-D_3 Caplets had only been doing as instructed by ProStrakan. The Appeal Board thus ruled no breach of the Code.

An NHS and Muslim affairs advisor to a healthcare management company, complained about the use of the term Halal to describe Adcal-D_3 Caplets (calcium carbonate and vitamin D3) by ProStrakan UK Limited.

COMPLAINT

The complainant stated that in his capacity as a Muslim affairs specialist and working with the community and voluntary sector he had received a number of enquiries from members of the community about the term Halal being loosely used for Adcal-D_3 Caplets.

Local Imams and various community activists in areas populated by Muslims had vehemently questioned this claim. Making such claims could lead to community tension, hence the need to contact the PMCPA to assist in averting any repercussions for the local health community.

The complainant understood that representatives from ProStrakan, not just locally, but regionally and nationally, had made the assertion without the necessary approval on the Halal status of Adcal-D_3 Caplets. Approvals of this nature were in most cases

made by the relevant Halal certifying bodies, of which there were several in the UK, yet upon inquiry, it appeared that none had granted ProStrakan any kind of certification for Adcal-D_3 Caplets.

The complainant submitted that this clearly was a very worrying development and suggested that Adcal-D_3 Caplets had, during their manufacture, been deemed Halal; not only during preparation but that no animal trials were conducted in the manufacture of this medicine. Conducting animal trials on non-Halal animals and then including those very products in medicines and labelling them as Halal would be questioned by the most senior Muslim Jurists. Naturally if there was no alternative available to treat a person's condition it might be deemed appropriate to use, however that would be a decision for a Muslim with the relevant expertise on Halal/Haram matters.

The complainant raised a number of questions regarding the Halal status of Adcal-D_3 Caplets.

Following a request from the case preparation manager for additional information the complainant stated that he had been informed by a number of local GPs that the ProStrakan representative had informed GPs of Adcal-D_3 Caplets' Halal status. A deputy director of medicines management at a primary care trust had also heard from some GPs that they believed Adcal-D_3 Caplets were suitable for Muslims.

When writing to ProStrakan, the Authority asked it to respond in relation to Clauses 7.2, 7.4, 9.1, 15.2 and 15.9 of the Code.

RESPONSE

ProStrakan stated that it took its responsibilities under the Code very seriously, and appreciated the opportunity to address the concerns raised by the complainant.

As an organisation with the capacity to influence the health and wellbeing of patients, ProStrakan held the views of its customers, and the wider community, in very high regard. It submitted that it had always endeavoured to ensure that the information provided to these groups was clear, accurate and appropriate. However, it would appear that in this instance some confusion had arisen with respect to the use of the term Halal in connection to Adcal-D_3 Caplets.

ProStrakan had never sought to promote Adcal-D_3 Caplets as Halal. The term did not appear on any promotional materials. The promotional campaign that supported the launch was centred on the swallowability of the caplet itself, a claim that was intended to counter patient concerns about the unpalatable nature of certain calcium supplements.

However, the company believed that some confusion had arisen as a consequence of the gelatin free status of the new caplets. As the caplet itself was gelatin free, and the vitamin D in the product was derived from a Halal source, this might have led to the misconception that the caplet itself was Halal.

As a consequence and to ensure that no further confusion arose, a telecon was held on the 28 February 2012 between the field based management team and the senior vice president, commercial operations, in order to clarify the conditions under which the term Halal might be used in relation to the caplets. This telecon was used to further reinforce the importance of accurately communicating the characteristics of the product.

ProStrakan submitted that the caplets and associated promotional materials were launched during the annual sales conference in September 2011. No promotional materials contained a claim that Adcal-D_3 Caplets were Halal. Copies of the current promotional materials and of representatives' briefing material were provided. ProStrakan submitted that the key selling messages for Adcal-D_3 Caplets were centred on ease of swallowing and clinical evidence, a fact reinforced by the documentation discussed above. Promoting the medicine as a Halal option was never an aim or intention. Only one section of the briefing document referred to the term Halal; the paragraph which discussed the sales aid stated:

> 'A key feature which will appeal to many patients is that Adcal-D_3 Caplets are gelatin free, and therefore suitable for vegetarians, and patients adhering to strict halal diets.'

This was included in the briefing document to equip representatives with the necessary information to respond to questions from health practitioners about patients with dietary restrictions. It was intended to allow representatives to explain that the medicine was gelatin free and so could be an alternative for patients with strict religious backgrounds given that the vitamin D component of Adcal-D_3 Caplets was certified as Halal. The oral brief accompanying this document made it clear that this was an issue that must be considered on a case-by-case basis between the doctor and their patient.

When taken in consideration with the rest of ProStrakan's materials, and the remainder of the briefing document, it was clear that the promotion of Adcal-D_3 Caplets as a Halal option was not advocated. ProStrakan therefore denied a breach of Clause 15.9.

The representative responsible for the area at issue was interviewed as were his manager and the partnership development executive (PDE) for the region.

The representative in question had considerable experience in the industry and treated the distinction between Halal and Haram substances with the utmost respect. When interviewed the representative stated that, while he had discussed Adcal-D_3 Caplets with customers, he had never claimed that the caplet itself was Halal; although the term Halal had been discussed this was in response to customer questions regarding the source of the vitamin D, which he understood had a Halal certificate.

The representative's account of events was confirmed by both his manager and the PDE responsible for his territory. Both had monitored the representative in a number of calls, but neither had observed him making inappropriate claims concerning the Halal status of the product. This view was backed up by his call records. No calls held with customers since the launch of Adcal-D_3 Caplet referred to the product as Halal, or indicated that it had been promoted to customers as such. Given this evidence ProStrakan denied a breach of Clause 15.2.

ProStrakan had not conducted any animal trials on the product.

ProStrakan stated that it was never its intention to promote Adcal-D_3 Caplet as a Halal product and therefore no approval was sought from Muslim scholars or other bodies which regulated the use of the term. Had it been the intention to promote the product in this fashion it would, as a matter of course, have engaged with the community to ensure that its required standards were met.

With regard to whether patients made aware of the Halal status, ProStrakan submitted that the patient education leaflet supporting the medicine did not use the term Halal. No direct to patient advertising for Adcal-D_3 Caplets was produced for patients as this was prohibited by the Code.

ProStrakan did not know how many patients had taken Adcal-D_3 Caplets on the assumption that it was Halal as the collection of information on patient prescriptions was prohibited by the Code.

ProStrakan submitted that documentation had been provided from a Halal certifying body certifying the vitamin D component of Adcal-D_3 Caplets. However, this certification was not actively sought by ProStrakan. The certificate was provided as standard by the organisation responsible for producing the product.

ProStrakan stated that as it had not promoted the product as Halal, no attempt had been made to contact the NHS regarding this matter.

ProStrakan submitted that as noted above, none of the promotional materials contained the claim that Adcal-D_3 Caplets were Halal. Nor had the company sought to verbally make claims regarding the product that it was unable to substantiate.

ProStrakan therefore denied breaches of Clauses 7.2 and 7.4.

ProStrakan stated that it endeavoured to follow both the spirit and the letter of the Code, and as such it had made every effort to address the complainant's concerns to the fullest degree possible. The company was concerned to hear that misunderstandings appeared to have occurred in relation to the Halal status of the caplets, and had already taken steps to address this.

The company submitted that its inquiry had established that the promotion of the Adcal-D_3 Caplets complied with the Code. It had never promoted the medicine as a Halal option, as was evidenced by the materials supporting the medicine and the investigation detailed above. ProStrakan thus denied a breach of Clause 9.1.

PANEL RULING

The Panel noted ProStrakan's submission that some confusion had arisen as a consequence of the gelatin free status of the new caplets used in Adcal-D3. That, together with the fact that the vitamin D in the medicine was derived from a Halal source, might have led to the misconception that the caplets were Halal. ProStrakan provided a copy of a certificate from a certifying body with regard to the vitamin D component of the Adcal-D_3 Caplets.

The Panel noted ProStrakan's submission that no promotional material for Adcal-D_3 Caplets contained a claim about the suitability of the medicine for Halal diets and that promotion of the medicine as a Halal option was never its aim or intention. Most of the promotional material provided referred to the fact that Adcal-D_3 Caplets were gelatin free; none of it referred to the medicine being suitable for those following a Halal diet. The Panel noted however that a briefing document for representatives entitled 'Key Account Team Brief – Adcal-D_3 Caplet Campaign' (ref M004/0018) contained the statement in relation to the first page of the sales aid that 'A key feature which will appeal to many patients is that Adcal-D_3 Caplets are gelatin free, and therefore suitable for vegetarians, and patients adhering to strict halal diets'.

The Panel noted ProStrakan's submission that this was included in the briefing document to help representatives respond to questions from health professionals about patients with dietary restrictions. It was intended to allow representatives to explain that the product was gelatin free and as such could provide an alternative for patients with strict religious backgrounds given that the vitamin D component of Adcal-D_3 Caplets was certified as Halal.

In the Panel's view, although the caplets were gelatin free and the vitamin D was derived from a Halal source, Adcal-D_3 Caplets as a product were not granted Halal status. The Panel considered that the claim in the briefing document that Adcal-D_3 Caplets were suitable for patients adhering to strict Halal diets was misleading. It was not made sufficiently clear that only the vitamin D component of the medicine was certified as Halal. A breach of Clause 7.2 was ruled. The Panel considered that the claim was not capable of substantiation and a breach of Clause 7.4 was ruled. The briefing material advocated a course of action that was likely to lead to a breach of the Code. A breach of Clause 15.9 was ruled. Further, the company had failed to maintain high standards in this regard and a breach of Clause 9.1 was ruled.

With regard to the activity of the representative in question, the Panel noted that the parties' accounts differed. The complainant had referred to second and third hand reports that the representative had discussed the Halal status of Adcal-D_3 Caplets. No details of the discussions were provided. ProStrakan submitted that the representative had stated that while he had discussed Adcal-D_3 Caplets with customers he had never claimed that the caplet itself was Halal; the term Halal had been discussed but only in response to customer questions about the source of the vitamin D, which he understood had a Halal certificate. As noted above, however, the representatives' briefing material stated that Adcal-D_3 Caplets were suitable for patients on a strict Halal diet and so in that regard the Panel considered that on the balance of probabilities the representative had implied that the medicine had been granted Halal status. Although the representative had used material provided by the company and followed company instructions all the relevant requirements of the Code had not been complied with. A breach of Clause 15.2 was ruled.

APPEAL BY PROSTRAKAN

ProStrakan submitted that it had never made any promotional claims regarding the Halal status of Adcal-D_3 Caplets as evidenced by its previous provision of, *et al*, a detail aid, two leavepieces and two advertisements none of which made such claims.

ProStrakan submitted that the briefing document entitled 'Key Account Team Brief – Adcal-D_3 Caplet Campaign', developed to help representatives respond to questions from health professionals, contained the statement 'A key feature which will appeal to many patients is that Adcal-D_3 Caplets are gelatin free, and therefore suitable for vegetarians, and patients adhering to strict halal diets'. Although ProStrakan's previous response indicated that Adcal-D_3 Caplets were gelatin free and the vitamin D component in the medicine was derived from a Halal source, the statement in the briefing document was nonetheless ruled to be in breach of Clauses 7.2, 7.4, 15.9 and 9.1. This ruling was made on the basis that Adcal-D_3 Caplet as a product had not been granted Halal status despite the fact that the caplets were gelatin free and the vitamin D component was derived from a Halal source.

ProStrakan took this matter very seriously. Out of respect for the concerns of the complainant in this case, the PMCPA, health professionals throughout the UK and not least to Muslim patients, it had tried to resolve this matter by providing definitive evidence regarding the Halal status of Adcal-D_3 Caplet. This matter was particularly important given the therapeutic needs of Muslim patients who, given Shariah dress requirements and Halal dietary restrictions, might be at particular risk of calcium and vitamin D deficiency and for whom there might be limited therapeutic options due to the same Halal restrictions. To this effect ProStrakan had worked closely with a body that sanctioned the Halal status of products.

ProStrakan submitted that this body thoroughly reviewed its procedures and facilities in line with the above criteria. Subsequent to that review the Adcal-D_3 Caplet (including all ingredients) as supplied to the UK from the manufacturing site in Germany, which had also been fully audited by the body, had been Halal certified as in accordance with Islamic Shariah Law and as suitable for use by Muslims. A copy of the Halal certificate of authentication and the Halal certification record for Adcal-D_3 Caplet was provided. As the manufacturing authorization and product specification of Adcal-D_3 Caplet was both tightly regulated by the appropriate competent authorities and unmodified since the UK launch in September 2011, ProStrakan therefore appealed the Panel's rulings with regards to Clauses 7.2, 7.4, 15.9 and 9.1 as Adcal-D_3 Caplets were indeed Halal and had been since their UK launch. The briefing document was thus not misleading, it could be substantiated and did not advocate a course of action likely to lead to a breach of the Code and consequently ProStrakan had maintained high standards.

ProStrakan submitted that with regard to the activity of its representative and the ruling of a breach of Clause 15.2, the representative in question had never claimed that Adcal-D_3 Caplets were themselves Halal. Indeed, no first hand evidence to the contrary had been provided to substantiate this complaint. However, given that Adcal-D_3 Caplets had been certified as Halal by a certifying body, the briefing document issued to the representative in question was neither misleading nor incapable of substantiation on this point, nor did it advocate a course of action that was likely to lead to a breach of the Code. ProStrakan consequently appealed the ruling of a breach of Clause 15.2 and submitted that the representative in question had at all times maintained a high standard of ethical conduct in the discharge of his duties and had complied with all relevant requirements of the Code.

In summary, ProStrakan submitted that Adcal-D_3 Caplets had been Halal certified in accordance with Islamic Shariah Law and had been deemed suitable for use by Muslims. ProStrakan therefore appealed all of the Panel's rulings.

ProStrakan submitted that it had both a clinical and ethical obligation to appeal as the Halal diet and Shariah dress requirements might put Muslim patients, especially women, at increased risk of osteoporosis, and increased the clinical need for therapeutic supplementation of malnutrition for example in pregnancy and in established vitamin D dependent osteomalacia. Since the requirements for Halal limited the treatment options for Muslim patients in this therapy area, hence the nature of this complaint, ProStrakan submitted it would be wrong for it to let the rulings in the case go unchallenged. Indeed, ProStrakan was concerned that the Panel's rulings might make health professionals think that Adcal-D_3 Caplets were not Halal, which was not the case, and that as an unintended consequence of these rulings, an important and high risk section of the community might be inappropriately deprived of a licensed medicine from which it might benefit.

RESPONSE FROM THE COMPLAINANT

The complainant provided witness statements, (one from a pre-registration pharmacist and a pharmacy manager, one from a deputy director, medicines management and one from a pharmacist) which referred to ProStrakan representatives discussing the Halal status of Adcal-D_3 Caplets with local health professionals. The complainant alleged that this had in some instances confused not only health professionals but also, more importantly, Muslim patients.

The complainant noted the claim in the ProStrakan briefing document 'A key feature which would appeal to many patients was that Adcal-D_3 Caplets were gelatin free, and therefore suitable for vegetarians, and patients adhering to strict halal diets'. The complainant alleged that gelatin free and Halal had completely different connotations, therefore, this again was very confusing. The complainant queried what ProStrakan understood by a 'strict Halal diet'.

ProStrakan, in its response to the complaint, acknowledged that this misconception had arisen from the fact that only the vitamin D in the Adcal-D_3 Caplet was Halal, consequently, between the response to the complaint and the appeal the product had been granted full Halal status. The complainant welcomed submission of evidence to the Appeal Board that supported this.

Further, the complainant noted ProStrakan's reference to confusion having occurred and as a result, and without the necessary jurisprudential guidance, clarified to the field based management team under what conditions the term Halal could be used, and, again, the complainant welcomed the necessary evidence, which allowed ProStrakan to use the term Halal.

The complainant noted that in its response ProStrakan had stated that it had never intended to promote Adcal-D_3 Caplet as a Halal product and therefore no approval was sought from Muslim Scholars or other bodies which regulated the use of the term. Additionally, ProStrakan had cited certification from one body but in its appeal had included certification from another. The complainant queried why the latter certification was omitted from ProStrakan's response to the complaint.

The complainant submitted that the community was now utterly perplexed because it had two different sanctioning bodies, with conflicting reports, one which claimed that the vitamin D component of Adcal-D_3 Caplets was Halal and the other which suggested the whole Adcal-D_3 Caplet was Halal. The complainant queried how this process was undertaken, particularly given that the first body would only certify the vitamin D component of the Adcal-D_3 Caplet as Halal.

The complainant stated that in his view ProStrakan representatives, in their contact with health professionals, had shown the highest degree of unethical behaviour towards the health community and particularly Muslim patients. The Halal certificate provided by the first body clearly suggested the vitamin D was provided by a nutrition company. Was this company a part of ProStrakan? There was no basis from this certification for Adcal-D_3 Caplets to be considered Halal, when only the vitamin D component was Halal certified. There was no mention of Adcal-D_3 Caplets being Halal certified.

ProStrakan appeared to suggest that Muslims had wholly different therapeutic needs to the wider indigenous population. ProStrakan had also stated that Muslims, given Shariah dress requirements and Halal dietary restrictions, might be at particular risk of calcium and vitamin D deficiency. The complainant stated that he would welcome any evidence to corroborate this claim. ProStrakan suggested, for the same reason, that there might be limited therapeutic options due to Halal restrictions. Observing a Halal code did not restrict nor limit therapeutic options; on the contrary, it empowered patients to make informed decisions and provided guidance on a holistic approach to life. ProStrakan suggested it had a close working relationship with the second body which provided Halal certification for Adcal-D_3 Caplets. This organisation had no track record of providing Shariah compliant services, locally, regionally or nationally, and had only been registered for fourteen months, furthermore for only seven months when Adcal-D_3 Caplets were launched.

The complainant alleged that the most fundamental point and the crux of this matter was, what schools of Madhhab (law) were consulted prior to gaining Halal certification? The complainant listed eight and noted that the principles that should govern Halal certification of any medicine for Muslim patients might differ from school to school.

The complainant stated that in his view, prior to and including the September launch date of Adcal-D_3 Caplets, no real and meaningful attempts were made by ProStrakan to consult appropriately with the significant Halal bodies in the UK.

The complainant noted that it was further suggested by ProStrakan that the second body conducted a 'thorough' review of ProStrakan procedures and facilities. No evidence had been submitted to substantiate this claim.

The complainant alleged that evidently, from the witness statements provided, it should be considered whether the ProStrakan representative had made unsubstantiated claims of the Halal status of Adcal-D_3 Caplets, therefore confusing the health community and Muslim patients.

The complainant emphasised that there was no irrefutable evidence of the Halal status of Adcal-D_3 Caplets.

The complainant stated that he would welcome any evidence which supported ProStrakan's claim that by observing a Halal diet and Shariah dress

requirements, Muslim women were especially at risk of osteoporosis. Indeed, there were several options available to patients who might be at risk of osteoporosis and if there was no Halal option available a non-Halal option, to preserve life and wellbeing, could be offered. Therefore to suggest, without the necessary clinical evidence, because a Muslim woman dressed in line with Shariah, she was at increased risk of osteoporosis was wholly unacceptable.

The complainant urged the Appeal Board to uphold the rulings of the breaches of the Code.

APPEAL BOARD RULING

The Appeal Board noted the statement 'A key feature which will appeal to many patients is that Adcal-D_3 Caplets are gelatin free, and therefore suitable for vegetarians, and patients adhering to strict halal diets' in the representatives' briefing document entitled 'Key Account Team Brief – Adcal-D_3 Caplet Campaign'. The briefing material was dated August 2011. The Appeal Board noted from ProStrakan that this statement had been included to equip representatives with a means to respond to questions from health professionals; the company did not expect the representatives to use the claim promotionally.

In the Appeal Board's view, ProStrakan's submission that none of its promotional material had ever included claims regarding the Halal status of Adcal-D_3 Caplets was inaccurate given the statement in the briefing document. The Appeal Board considered that briefing material was part of the promotional material for the product and was concerned that ProStrakan did not consider it to be so. The statement in the briefing material was clearly a promotional claim that Adcal-D_3 Caplets were Halal. Describing something as a 'key feature' would have highlighted its importance as a point for the representatives to note.

The Appeal Board considered that given the sensitivity of claims regarding the Halal status of medicines and their importance to particular health professionals and patients such statements needed to be clear and accurate so there was no potential to mislead. The statement in the briefing document implied that Adcal-D_3 Caplets were Halal as a consequence of being gelatin free. The Appeal Board's understanding was that Halal status was more than the absence of gelatin.

The Appeal Board considered that although the caplets were gelatin free and the company had a certificate (dated 22 November 2011) that stated that the vitamin D component met the Halal requirements, it did not have a certificate when the briefing material was prepared in August 2011 to show that Adcal-D_3 Caplets were Halal. The certificate from the second body was dated 20 April 2012. The Appeal Board considered, therefore, that when the claim in the briefing document that Adcal-D_3 Caplets were suitable for patients adhering to strict Halal diets was approved it was misleading, not capable of substantiation and advocated a course of action that was likely to lead to a breach of the Code and it upheld the Panel's rulings of breaches of Clauses 7.2, 7.4 and 15.9. Further, the company had failed to maintain high standards in this regard and the Appeal Board upheld the Panel's ruling of a breach of Clause 9.1. The appeal on these points was unsuccessful.

The Appeal Board considered that the representative in question who had used the briefing document to refer to the Halal status of Adcal-D_3 Caplets had only been doing as instructed by ProStrakan. The Appeal Board thus ruled no breach of Clause 15.2. The appeal on this point was successful.

Complaint received **24 February 2012**

Case completed **21 June 2012**

CASE AUTH/2482/2/12

ANONYMOUS v NOVO NORDISK

Invitation to a meeting

An anonymous, contactable complainant described as disturbing an email invitation to a Novo Nordisk satellite symposium entitled 'Weighing up the benefits: the practical use of GLP-1 [glucagon-like peptide-1] receptor agonists and modern insulins in tackling type 2 diabetes' due to be held at the Diabetes UK 2012 meeting. Two of the topics to be discussed would be individualisation of GLP-1 receptor agonist treatment and benefits of insulin analogues, focusing on hypoglycaemia. The invitation asked readers to register on-line and included a link to the Victoza (liraglutide) prescribing information.

Novo Nordisk marketed Victoza (a GLP-1 receptor agonist) as add-on therapy for adults with type 2 diabetes who had failed to achieve glycaemic control with oral antidiabetic therapy. Victoza was not licensed for use in combination with insulin. Novo Nordisk also marketed Levemir (insulin detemir) which had recently been granted a licence extension such that it could now be used in combination with Victoza.

The complainant noted that he/she had subscribed to a medical educational website from Novo Nordisk but not to promotional messages. The email at issue pointed to a symposium which promoted off label use of Victoza in combination with insulin (the linked prescribing information did not include a combination with insulin). The prescribing information for Novo Nordisk's insulins was not available to check. The website also only had prescribing information for Victoza so it was not clear that this was a promotional activity. The complainant noted that the registration website seemed open to everyone, not just doctors. The complainant did not consider that this was a legitimate activity.

The detailed response from Novo Nordisk is given below.

The Panel noted the complainant's submission that he/she had subscribed to a medical educational website but not to promotional messages. The homepage of the website stated that the site was for health professionals only and that they could obtain unlimited access to information, resources and tools about diabetes. The registration page of the website included the statement 'We would like to send you information about our products and services. I agree to be contacted by Novo Nordisk by post, telephone, email and SMS'. To the left of this was a box which was to be ticked to indicate agreement. The Panel noted that a request for permission to send promotional material had to be abundantly clear. The Panel did not consider that this requirement had been met and thus a breach of the Code was ruled.

The Panel noted Novo Nordisk's submission that the symposium at issue did not discuss the use of liraglutide in combination with insulin. The invitation and agenda (which could be obtained via an electronic link in the invitation) showed that GLP-1 receptor agonists and insulin analogues (modern insulins) were to be discussed as two separate topics. The Panel noted that the complainant had not provided any evidence that the use of liraglutide in combination with insulin would be discussed at the symposium. No breach of the Code was ruled.

The Panel noted Novo Nordisk's submission that as it had only one GLP-1 receptor agonist, Victoza, the prescribing information was included. The Panel further noted Novo Nordisk's submission that it marketed three insulin analogues (Levemir, NovoRapid and NovoMix), but as the invitation did not refer to any by name, no prescribing information for any insulin was included. The Panel did not consider that the email promoted any particular insulin and thus no prescribing information for insulin was required. There was no disguised promotion of any insulin. No breaches of the Code were ruled. These rulings were upheld on appeal by the complainant.

The Panel noted the complainant's submission that the registration website appeared to be open access and not restricted to health professionals. The Panel noted Novo Nordisk's submission that the website was password protected and not accessible by the public. Health professionals who wished to access the site had to create an account by providing, *et al*, a professional registration number. Once registered a username and password were provided. The Panel noted that the registration page of the website, which anyone could access, contained no product or other clinical or promotional material. The Panel considered that in terms of access the website at issue complied with the Code. No breach of the Code was ruled. The Panel did not consider that the website promoted a prescription only medicine to the public and ruled no breach of the Code. These rulings were upheld on appeal by the complainant.

An anonymous, contactable complainant complained about an email invitation (ref UK/DB/0112/0028b) to a forthcoming Novo Nordisk satellite symposium entitled 'Weighing up the benefits: the practical use of GLP-1 [glucagon-like peptide-1] receptor agonists and modern insulins in tackling type 2 diabetes' which was to be held at the Diabetes UK 2012 meeting. The invitation stated that two of the topics to be discussed would be

individualisation of GLP-1 receptor agonist treatment and benefits of insulin analogues, focusing on hypoglycaemia. The invitation asked readers to register on-line. A link to the Victoza (liraglutide) prescribing information was included.

Novo Nordisk Limited marketed Victoza (a GLP-1 receptor agonist) as add-on therapy for adults with type 2 diabetes mellitus who had failed to achieve glycaemic control with oral antidiabetic therapy. Victoza was not licensed for use in combination with insulin. Novo Nordisk also marketed Levemir (insulin detemir) which had recently been granted a licence extension such that it could now be used in combination with Victoza.

COMPLAINT

The complainant described the email as rather disturbing. He/she had subscribed to a medical educational website from Novo Nordisk (novomedlink.co.uk) but not to promotional messages. The email at issue pointed to a symposium which promoted off label use of Victoza in combination with insulin (the complainant noted that the link to prescribing information at the bottom of the email did not include a combination with insulin). The complainant stated that Novo Nordisk also sold insulin but the prescribing information for these was not available to check. The website also only had prescribing information for Victoza so it was not clear that this was a promotional activity. The complainant noted that the registration website seemed open to everyone, not just doctors. The complainant did not consider that this was a legitimate activity.

When writing to Novo Nordisk, the Authority asked it to respond in relation to Clauses 3.2, 4.1, 9.9, 12.1, 22.1 and 24.1 of the Code.

RESPONSE

Novo Nordisk explained that it owned and managed the website NovoMedLink which was an online resource for health professionals with an interest in diabetes. The website provided promotional and non-promotional information on all aspects of diabetes.

The website was password protected and was not accessible by the public. Health professionals who wished to access NovoMedLink had to create an account by providing standard personal details including a General Medical Council (GMC) number or nurse equivalent. Once registered, the health professional was given a username and password in order to access the site.

A screen print of the registration page of NovoMedLink was provided. Novo Nordisk submitted that this screen was displayed and completed when a health professional registered to the site. A section of the screen print was highlighted which Novo Nordisk stated clearly indicated that registered users who selected the tick box agreed to receive information on Novo Nordisk products and services. This was also the case if a health professional registered to the site via a paper based system. Novo Nordisk submitted that as the complainant's details were unknown, it could not check whether he/she selected this box. However, the company was confident that it had a robust system to ensure that only users who had selected this box would receive such updates.

Novo Nordisk submitted that the invitation at issue was emailed on 24 February 2012 to all registered users of the NovoMedLink site who had agreed to receive such information upon registering with the website. A similar invitation was also distributed by hand to health professionals by the diabetes sales force.

Novo Nordisk stated that a link to the Victoza prescribing information was included on the invitation and the symposium registration website because the agenda referred to 'GLP-1 receptor agonists'. As Novo Nordisk only marketed one GLP-1 receptor agonist, Victoza could be identified. Prescribing information for the modern insulins had not been made available. Novo Nordisk submitted that it marketed several modern insulins, as did competitors, and there was no way to link the content of the symposium to a certain type of insulin. Since no specific insulin could be identified Novo Nordisk considered that there was no requirement for prescribing information for the modern insulins to be made available on the invitation or the symposium registration website.

Novo Nordisk submitted that its symposium at the Diabetes UK 2012 meeting was promotional. The three distinct topics which would be covered were GLP-1 receptor agonists, real life data and the importance of patient choice and the benefits of insulin analogues (modern insulins), focussing on hypoglycaemia.

Data around the use of combining liraglutide and a modern insulin as a treatment for diabetes were not discussed during this symposium. Novo Nordisk was therefore unclear as to why the complainant had alleged that the symposium would promote off label use of Victoza in combination with insulins but assumed that he/she might have misinterpreted the title of the symposium 'Weighing up the benefits: the practical use of GLP-1 receptor agonists and modern insulins in tackling type 2 diabetes'. As stated above, the agenda had been arranged to discuss GLP-1 receptor agonists and insulin analogues (modern insulins) in the treatment of diabetes as separate topics and not the use of GLP-1 receptor agonists in combination with modern insulins'.

Novo Nordisk noted, however, that its insulin analogue, Levemir recently received a licence update for add-on therapy to liraglutide treatment.

Novo Nordisk submitted that access to the symposium website was limited, as only health professionals who had received the invitation to the symposium via NovoMedLink or via a representative had been told about it. The registration website was

wholly directed to health professionals and the public had not been encouraged to access it.

Based on the above information, Novo Nordisk denied any breach of Clauses 22.1, 24.1, 12.1, 9.9, 4.1 or 3.2.

PANEL RULING

The Panel noted the complainant's submission that he/she had subscribed to a medical educational website from Novo Nordisk, novomedlink.co.uk, but not to promotional messages. The homepage of the website stated that the site was for health professionals only and that they could obtain unlimited access to information, resources and tools about diabetes for them and their patients. The Panel noted that the registration page of the website had, below the registration details required, the statement 'We would like to send you information about our products and services. I agree to be contacted by Novo Nordisk by post, telephone, email and SMS'. There was a box to the left of this statement which was to be ticked to indicate agreement to this. The Panel noted that it had previously been established that text requesting permission to send promotional material had to make it abundantly clear that the intention was to send promotional material from pharmaceutical companies. The Panel did not consider that this requirement had been met in this case. A breach of Clause 9.9 was ruled.

The Panel noted Novo Nordisk's submission that the symposium at issue did not discuss the use of liraglutide in combination with insulin as a treatment for diabetes. The invitation and agenda, which could be obtained via an electronic link in the invitation, showed that GLP-1 receptor agonists and insulin analogues (modern insulins) in the treatment of diabetes were to be discussed as two separate topics ie 'Individualisation of GLP-1 receptor agonist treatment' and 'Benefits of insulin analogues, focusing on hypoglycaemia'. The Panel noted that the complainant had not provided any evidence that the use of liraglutide in combination with insulin would be discussed at the symposium. No breach of Clause 3.2 was ruled.

The Panel noted Novo Nordisk's submission that the email invitation to the symposium referred to GLP-1 receptor agonists and as Novo Nordisk marketed only one such medicine, Victoza, the prescribing information was included. The Panel further noted Novo Nordisk's submission that although it marketed three insulin analogues (Levemir, NovoRapid (insulin aspart)and NovoMix (biphasic insulin aspart)), the invitation did not refer to any by name and so it did not include prescribing information for any of its insulins. The Panel did not consider that the email promoted any particular insulin and thus no prescribing information for insulin was required. No breach of Clause 4.1 was ruled. There was no disguised promotion of any insulin, and no breach of Clause 12.1 was ruled. These rulings were appealed by the complainant.

The Panel noted the complainant's submission that the registration website appeared to be open access and not restricted to health professionals. The Panel noted Novo Nordisk's submission that the website was password protected and not accessible by the public. Health professionals who wished to access NovoMedLink had to create an account by providing standard personal details including a professional registration number. Once registered a username and password were provided so that a health professional could access the site. The Panel noted that the registration page of the website, which anyone could access, contained no product or other clinical or promotional material. The Panel considered that in terms of access the website at issue complied with the Code. No breach of Clause 24.1 was ruled. The Panel did not consider that the website promoted a prescription only medicine to the public and ruled no breach of Clause 22.1. These rulings were appealed by the complainant.

APPEAL FROM THE COMPLAINANT

The complainant considered that there was some confusion as to his/her complaint about websites. The one he/she was not happy with was novonordisksymposium.com, which then redirected to the registration details for the symposium and the agenda and differed substantially from the email in that it had a lot more emphasis on liraglutide. This page was freely accessible; it was not an obscure link but one that might come up during searches. Indeed, it still popped up on a Google search. The complainant provided a screenshot and the last 'link' on that page was to the symposium. As the initial email displayed this link in large font the complainant queried whether Novo Nordisk wanted people to actively go to that site for future symposia. The link was designed to be easily remembered; in the complainant's view it should also be protected either by password or some form of registration. If Novo Nordisk really wanted it to be kept quiet, it should have stuck to the more obscure address which the site redirected to. That would have meant it would not be searchable on Google and would not encourage advertising to the public.

The complainant alleged that the description of the event on the email, with no mention of the medicine Novo Nordisk was overtly promoting, was misleading. The complainant expected the Victoza product logo to appear on the email so he/she would know whether or not to click on the link.

As for the lack of clarity of insulins, the complainant also did not accept the Panel's ruling. The title clearly referred to 'modern insulins'. Novo Nordisk blatantly meant its basal insulin [Levemir], the other products were more than ten years old. The mix version was just a combination of an old medicine. So Novo Nordisk was very clear that only modern insulins would be discussed. Being one of two, it was disingenuous of Novo Nordisk to pretend its product would not be discussed.

The complainant appealed the Panel's rulings of no breach of Clauses 4.1, 12.1 and 22.1.

The complainant further appealed the ruling of no breach of Clause 24.1 because the open access novonordisksymposium.com contained overtly promotional material.

COMMENTS FROM NOVO NORDISK

Novo Nordisk disagreed that the agenda provided on the email invitation differed substantially to the agenda provided on the symposium registration website. The invitation provided recipients with an overview of the symposium so that they could decide whether they wanted to attend. The symposium registration website provided further detail on the agenda topics to be covered and was not inconsistent with the emailed agenda. Given the email invitation referred to GLP-1 receptor agonist treatment and contained a link to Victoza prescribing information, it was obvious that data regarding Victoza would be covered in the symposium.

Novo Nordisk reiterated that access to the symposium website was limited as only health professionals who were invited to the symposium via NovoMedLink or by a representative were told about it. The website was wholly directed to health professionals and the public was not encouraged to access it.

Novo Nordisk submitted that there had to be a deliberate search for the registration website using composite search criteria, ie linking Novo Nordisk with the scientific congress. Therefore Novo Nordisk disagreed that the site was 'freely accessible' and would pop up on a Google search.

Novo Nordisk submitted that it was self-evident that invitations to an event had to clearly inform delegates how they could register for the event if they wanted to attend. Highlighting the website address in large font on the email invitation was not unacceptable under the Code.

Novo Nordisk submitted that each symposium it organised had its own invitation detailing how to register for the event online, via a weblink. Novo Nordisk did not expect health professionals to register for a future meeting based on memories of an old invitation. The website in question was no longer available.

Novo Nordisk submitted that the email invitation clearly stated GLP-1 receptor agonist treatment was a key topic within the symposium. Novo Nordisk only marketed one such medicine and so Victoza could be identified; a link to the Victoza prescribing information was included on the invitation. Novo Nordisk did not believe there was a mandatory requirement to include a product logo on an invitation of this nature.

Novo Nordisk submitted that the email invitation clearly stated what Novo Nordisk paid for in relation to this symposium, and so it was clear that this was a Novo Nordisk organised promotional event and that GLP-1 receptor agonist treatment, including Victoza, would be discussed. Novo Nordisk therefore disagreed that the agenda disguised the promotion of Victoza.

Novo Nordisk submitted that the complainant had stated that the only 'modern insulin' it marketed was a 'basal insulin'. In that regard Novo Nordisk explained that the term 'modern insulin' referred to all third generation insulins, ie all insulin analogues, and was very well recognised and regularly and widely used in the medical press and the electronic Medicines Compendium. As the terms 'modern insulins' and 'insulin analogues' could be used interchangeably both were referred to on the email invitation and the symposium registration website.

Novo Nordisk noted that it marketed three modern insulins, Levemir (basal insulin), NovoRapid and NovoMix. Novo Nordisk listed five other modern insulins marketed by other companies. Novo Nordisk therefore disagreed that 'modern insulin' only referred to its basal insulin.

Novo Nordisk submitted that, as previously stated, prescribing information for the modern insulins was not made available on the email invitation or the symposium registration website. As noted above, Novo Nordisk marketed several modern insulins, as did competitors, and the content of the symposium could not be linked to a certain type of insulin. Since no specific insulin could be identified Novo Nordisk submitted that there was no need for it to put the prescribing information for its modern insulins on the email invitation or the symposium registration website.

FINAL COMMENTS FROM THE COMPLAINANT

The complainant considered that Novo Nordisk had denied the obvious. The complainant alleged that the agenda as set out in the email was substantially different to what was on the webpage. The agenda in the email read:

'Topics will include:
- Individualisation of GLP-1 receptor agonist treatment
- Real-life data and the importance of patient choice
- Benefits of insulin analogues, focusing on hypoglycaemia'

The complainant provided a copy of the subsequent confirmation email.

The complainant stated that the agenda on the web page, which he/she had to type because the page was now removed from the web, was as follows (emphasis added by the complainant and the quotation is from the complainant's version):

'Registration and refreshments
Welcome and introduction
Individualising patient care with GLP-1 receptor agonists
Liraglutide in clinical practice
Liraglutide: a patient's perspective
What patients want

The benefit of **insulin analogues: clinical and economic impact of hypoglycaemia**
Questions to the panel
Summary and close.'

The complainant noted the marked difference between the agenda on the email and the website, with obvious emphasis on liraglutide. The complainant was not sure how Novo Nordisk considered this to be the same. The complainant noted that he/she received this email without the visit of a representative. Novo Nordisk stated that people who signed up to NovoMedLink were clear that they would receive promotional material. The Panel found this in breach. So, the fact that the email referred to an overtly promotional symposium was not made clear. The complainant submitted that he/she would not have clicked the link to find out more otherwise. It was an unbranded invitation at a major conference and the complainant expected a proper medical, balanced presentation with talks that dealt with all GLP-1s. The complainant noted that Novo Nordisk maintained that the mention of GLP-1 receptor agonist would imply Victoza but when it came to insulins, it did not make the same link.

The complainant alleged that the website was freely accessible to the public and that other health professional websites he/she visited either confirmed doctor/nurse status or asked for a GMC number etc. This would have solved the problem.

The complainant queried why the link to the website was in such large font. Why else would it be highlighted? It was obviously meant to remind readers to visit the page again. All the more reason to protect the access.

The complainant noted that, at first glance, the initial email only had the corporate livery, used broad terms and gave the impression of a scientific symposium. Instead, the agenda was highly focused only on Victoza. Why not use the Victoza logo? This was disguised promotion. Doctors should not have to look for a link to prescribing information to determine that something was promotional. It should be abundantly clear at first glance.

The complainant noted that Novo Nordisk had stated that it was addressing modern insulins and that the fact that it was not the only one on the market dispensed it from having to show prescribing information. The complainant disagreed; by its own admission, Novo Nordisk sold three of the eight modern insulins available.

The complainant continued to believe that Novo Nordisk had referred to its basal insulin. This was evident from the topic chosen 'The benefit of insulin analogues: clinical and economic impact of hypoglycaemia'. The hypoglycaemia benefit was a particular feature of basal insulins, not the other types. The complainant was annoyed that Novo Nordisk insisted that it had referred to eight insulin types, when it had obviously concentrated on basal insulins. So again, the omission of the Levemir logo and prescribing information was disguised promotion.

In summary, the complainant alleged that Novo Nordisk should have been much more transparent in its mass email to signed up NovoMedLink doctors (a breach of Clause 9.9 had been accepted) when promoting its symposium and that the email should have clearly referred to the emphasis on Victoza and Levemir with the logos of each clearly displayed.

APPEAL BOARD RULING

The Appeal Board noted that health professionals could sign up to novomedlink.co.uk to receive emails such as that received by the complainant. The Appeal Board noted from the representatives at the appeal that the purpose of the email was to provide 'top line' details on the symposium; if interested, the recipient could then follow the link at the end of the email to a separate registration website that provided a more detailed agenda and an option to register for the event. Novo Nordisk's sales representatives also provided health professionals who had not signed up to the website with the registration website details.

The Appeal Board noted that the invitation email had included the Novo Nordisk company logo indicating that Novo Nordisk had sponsored the symposium. The email referred to GLP-1 receptor agonists and as Novo Nordisk only marketed one of these, Victoza, the prescribing information was provided via a hyperlink. The Appeal Board noted that the email also mentioned modern insulins. As Novo Nordisk produced three insulin analogues (Levemir, NovoRapid and NovoMix) of the available eight and no particular insulin was identified, no prescribing information for any was provided. On the registration page, which also included the company logo, the agenda referred to liraglutide, and the prescribing information was again provided. Insulins were discussed but as none were identifiable no prescribing information was provided.

The Appeal Board considered that neither the email nor the registration page promoted any particular insulin and thus no prescribing information was required. The Appeal Board upheld the Panel's ruling of no breach of Clause 4.1. There was no disguised promotion of any insulin and from the initial email it was also clear that Novo Nordisk's GLP-1 receptor agonist, liraglutide, would be discussed. The Appeal Board upheld the Panel's ruling of no breach of Clause 12.1. The appeal on both points was unsuccessful.

The Appeal Board noted that by entering the correct combination in a composite Google search, the registration website could be returned. The Appeal Board considered that it was unfortunate that the registration website could be accessed by using only three search terms but considered that the likelihood of a member of the public accessing the registration website by this method was very low. Although it would have been preferable in this regard to manage

registration through novomedlink.co.uk directly, the Appeal Board considered that Novo Nordisk had taken reasonable steps. It did not consider that in this regard Novo Nordisk had promoted a prescription only medicine to the public. The Appeal Board upheld the Panel's ruling of no breach of Clause 22.1. The Appeal Board considered that in relation to access, the website complied with the Code and it upheld the Panel's ruling of no breach of Clause 24.1. The appeal on both points was unsuccessful.

Complaint received **25 February 2012**

Case completed **24 May 2012**

CASE AUTH/2488/3/12

LEAD PHARMACIST v MEDA

Email promotion of EpiPen

A lead pharmacist complained about an uninvited email from Meda, entitled 'Re. Adrenaline Autoinjectors & Patient Safety' which referred to confusion regarding the different administration techniques for the various auto-injectors. According to the email local GPs had suggested Meda contact the complainant to discuss the matter and that local clinicians had been led to believe that there was no difference in the administration method. The email referred specifically to the 'swing & jab' method of using EpiPen (marketed by Meda) and stated that there was no data to show what the clinical outcome would be if a 'place and push' auto-injector [ie Jext, marketed by ALK-Abelló] was administered in the manner of EpiPen. Meda was gravely concerned that inaccurate information about other auto-injectors having the same method of administration [as EpiPen] would cause confusion and put lives at risk.

The email seemed to imply that there were safety concerns with alternative products but the complainant knew of no evidence to substantiate this. The complainant stated that his local primary care trust (PCT) had not received any reports of concerns from GPs. The complainant alleged that the email constituted disguised promotion.

The detailed response from Meda is given below.

The Panel noted that the email referred to adrenaline auto-injectors and to EpiPen by name. It referred to adrenaline delivery at the point of a life threatening allergic emergency and the indication of anaphylaxis. It further stated that as EpiPen had been the auto-injector of choice for over 15 years, health professionals, carers and patients were familiar with its unique swing and jab method of administration. The Panel considered that the email was promotional.

The Panel considered that the title of the email, 'Re. Adrenaline Autoinjectors & Patient Safety', implied that it contained safety information rather than promotional messages. Email recipients would look at the title of an email before deciding when and whether to open it. The Panel noted that as the email was promotional its title rendered it disguised in that regard. A breach of the Code was ruled. This ruling was not appealed.

The Panel did not consider that the email implied that there were safety concerns *per se* with other adrenaline auto-injectors, but rather that there was confusion as to whether they could be administered in exactly the same way as EpiPen and that local GPs had suggested Meda contact the pharmacist. According to the email the confusion would put lives at risk. Given its view that the email did not imply there were safety concerns with the other adrenaline auto-injectors as alleged, the Panel considered that Meda did not need to substantiate this narrow point and thus ruled no breach of the Code. This ruling was not appealed.

The Panel noted that Meda had not provided any details of the 'local GPs' who had suggested it contact the complainant. Meda submitted that one health professional in the area recommended that it write to the pharmacist.

The Panel noted the documents issued by various PCTs, and provided by Meda to support its submission that there was confusion, were about each PCT's decision to change its auto-injector of choice from EpiPen to Jext. One document stated, *et al*, that Jext could be used 'exactly like an EpiPen' and documents from the other PCTs appeared to be very similar in that regard.

The Panel considered that it was extremely important that adrenaline auto-injectors were used correctly. It noted that although health professionals in some PCTs had been given information about the similarity of the administration of EpiPen and Jext none of the PCT documents were from the complainant's PCT. The identity of the complainant had not been disclosed to Meda. The company would know which PCTs had been sent the email in question. The Panel did not know what information the complainant's PCT had distributed regarding the change to Jext. The complaint was about the email from Meda and in that regard the Panel noted that it stated 'that there were no data to show what might happen if a "place and push…design of [adrenaline auto-injector] is administered in the manner of an EpiPen…'.

It appeared from Meda's own submission that one local GP had been concerned. This was inconsistent with the email which stated 'Local GPs have suggested for us to contact you to discuss this'. There was no evidence before the Panel to indicate that there were many local clinicians who had been led to believe that there was no difference in the administration method as stated in the email or that there was local confusion. The Panel considered that the email was misleading in this regard and the statement had not been substantiated and thus the Panel ruled breaches of the Code. These rulings were appealed by Meda.

The Panel noted that the Code required that, *et al*, email must not be used for promotional purposes, except with the prior permission of the recipient. No such permission had been granted by the complainant who referred to the email as 'uninvited' and a breach of the Code was ruled as

acknowledged by Meda. This ruling was not appealed.

The Appeal Board considered that Meda's submissions had been confusing and inconsistent but it noted that at the appeal further and better particulars had been produced to show that many GPs did not clearly understand the difference in the way that the various auto-injectors (notably EpiPen and Jext) should be administered. The Meda representatives stated that over forty GPs and pharmacists had expressed concern in this regard and between twelve and fifteen had asked Meda to write to PCTs about the matter. Taking all the circumstances into account the Appeal Board did not consider that the email was misleading on this point. No breach of the Code was ruled. In the Appeal Board's view the claim had been substantiated. No breach of the Code was ruled. The appeal on both points was successful.

A lead pharmacist complained about an uninvited email from Meda Pharmaceuticals Limited. The email was entitled 'Re. Adrenaline Autoinjectors & Patient Safety' and referred to confusion regarding the way of administering different auto-injectors. According to the email local GPs had suggested Meda contact the complainant to discuss the matter. The email stated that each adrenaline auto-injector had been designed with a substantially different administration technique. Meda believed that local clinicians had been led to believe that there was no difference in the administration method. The email referred specifically to the 'swing & jab' method of using EpiPen (an adrenaline auto-injector marketed by Meda) and as this had been the adrenaline auto-injector of choice for over 15 years, health professionals, patients and carers were very familiar with its use. The email stated that there was no data to show what would happen if a 'place and push' auto-injector [ie Jext, marketed by ALK-Abelló] was administered in the manner of the EpiPen and the subsequent impact on successful adrenaline delivery at the point of life threatening allergic emergency. Meda was gravely concerned that inaccurate information about other auto-injectors having the same method of administration [as EpiPen] would cause confusion and put lives at risk.

The email explained that Meda had written to the complainant about this matter at the suggestion of local GPs.

COMPLAINT

The complainant stated that he was instrumental in the recent local approval to use Jext. The email seemed to imply that there were safety concerns with alternative products but the complainant was not aware of any evidence to substantiate this. The complainant stated that he worked at the local primary care trust (PCT) and he knew that the PCT had not received any reports of concerns from GPs. The complainant alleged that the email constituted disguised promotion.

When writing to Meda the Authority asked it to respond in relation to Clauses 7.2, 7.4, 9.9 and 12.1 of the Code.

RESPONSE

Meda stated that the author of the email was recommended to write to the pharmacist concerned by a local health professional. This was stated in the email at issue although the health professional concerned was not named. Meda stated that it was surprised that the complainant had not received reports of concerns from local GPs as Meda had received such concerns from numerous GPs and other health professionals in various regions of the UK.

Meda submitted that the email attempted to make clear that adrenaline auto-injectors had different methods of administration and to point out that there had been repeated instances of confusion, whereby some prescribers believed they could be used in the same way. Evidence of this was provided in a letter from a PCT, which stated that 'Jext can be used exactly like an EpiPen'. In addition, another document from the same PCT, entitled 'Introducing Jext', stated that 'Jext and EpiPen share the same simple 2 step method of activation'. Meda submitted that this document had been used by three NHS organisations in a near identical format and the company had repeatedly raised this issue with the PMCPA to no avail (Cases AUTH/2462/12/11 and AUTH/2405/5/11, plus recent correspondence relating to the inaccurate promotion of Jext). The information in these PCT documents was incorrect and might be a serious risk to patient safety. Meda stated that it had also raised this matter with the PCT. Meda had attempted to highlight the differences between all three adrenaline auto-injectors in the UK market for the benefit of patient safety.

Meda submitted that the email's author took a responsible decision, at the suggestion of a health professional, to inform a senior pharmacist of these findings, who could convey this important information to local health professionals. The content of the email was factually correct and did not breach Clauses 7.2 or 7.4. The email was not intended to be promotional; it was written as factual information in support of the lead pharmacist's organisation and patient safety and was therefore not certified. If however the Panel considered that the email was promotional, then Meda apologised and acknowledged that as it was sent uninvited it would be in breach of Clause 9.9.

Meda did not believe that the email was disguised promotion. It was clear from which company the email had been sent, the product at issue and it presented factual information in an accurate and balanced manner. No attempt was made to claim an advantage for EpiPen over any competing device, nor were any features of EpiPen discussed except for the method of administration, which was the point of the email.

In Meda's view this situation would have been avoided if the PMCPA had taken a more serious view of ALK-Abelló's failure to accurately promote the method of administration of Jext. In the interest of patient safety, Meda wanted to ensure that EpiPen was administered with a swing and jab technique, Jext with a place and push technique and Anapen with a place and click technique, consistent with their marketing authorizations. An article published in The Pharmaceutical Journal helped to explain the importance of this matter (Holloway and Sharma 2012); in addition, a response to the article from a senior UK pharmacist supported the view that it was vital that pharmacists and patients were trained in the different methods of administration of the various auto-injectors (Jerman 2012). Meda urged the Authority to consider this information and the implications of failed administration of adrenaline in an anaphylactic emergency.

Following a request for further information, Meda submitted that it was made clear to the email's author during day to day contact with health professionals that they had significant concerns about the way Jext had been promoted in their region, which left many of them with the impression that Jext could be used in the same way as EpiPen. The evidence to support this was the PCT documents and others. The email's author was advised to contact the medicines management committee of the PCT to correct this false impression. The recipients of the email were identified through previous contact with them. The author of the email had routine contact with members of medicines management committees of various PCTs and so was known to the recipients before the email was sent. There were seven recipients, of whom five requested a meeting to discuss the points raised and appreciated the contact.

PANEL RULING

The Panel noted that the email at issue referred to adrenaline auto-injectors and to EpiPen by name. It referred to adrenaline delivery at the point of a life threatening allergic emergency and the indication of anaphylaxis. It further stated that 'EpiPen Auto-Injector has been the AAI [adrenaline auto-injector] of choice for over 15 years and as a result GPs, pharmacists, hospital doctors, nurses, caregivers and patients are all very familiar with its unique swing and jab method of administration'. Given the content of the email the Panel considered that it was promotional and found it difficult to understand how it could be viewed as anything other.

The Panel considered that the title of the email 'Re. Adrenaline Autoinjectors & Patient Safety', implied that it would contain safety information rather than promotional messages. Email recipients would look at the title of an email before deciding when and indeed whether or not to open such an email. The Panel noted its decision that the email was promotional and considered that the title of the email meant that it was disguised in that regard. A breach of Clause 12.1 was ruled. This ruling was not appealed.

The Panel did not consider that the email at issue implied as alleged that there were safety concerns *per se* with other adrenaline auto-injectors, but rather that there was confusion as to whether other such injectors could be administered in exactly the same way as EpiPen and that local GPs had suggested Meda contact the pharmacist. According to the email the confusion would put lives at risk. Given its view that the email did not imply there were safety concerns with the other adrenaline auto-injectors as alleged there was no need for Meda to provide evidence to substantiate this narrow point and thus the Panel ruled no breach of Clause 7.4. This ruling was not appealed.

The Panel noted that Meda had not provided any details of the 'local GPs' who suggested Meda contact the medicines management pharmacist. Meda submitted that one health professional in the area recommended that Meda write to the pharmacist.

The Panel noted the documents issued by various PCTs and provided by Meda in support of its submission that there was confusion. All communicated the decision of the relevant PCT to change its auto-injector of choice from EpiPen to Jext. One document issued by a PCT stated, *et al*, that Jext could be used 'exactly like an EpiPen'. This document also provided details of actions taken by the PCT, including training by the manufacturer to support the change from EpiPen. The documents from the other organisations appeared to be very similar. All were entitled 'Introducing Jext' and contained an image of the Jext 150mcg and 300mcg injection devices. In two of these documents the text on the injection devices which described the injection technique was visible. In a section 'Important point to remember' was the statement 'Jext and EpiPen share the same simple 2 step administration'. In addition the documents provided reasons for the change.

The Panel considered that it was extremely important that adrenaline auto-injectors were used in accordance with the instructions in the relevant summary of product characteristics (SPC). It noted that although some evidence had been supplied regarding information given to health professionals in various PCTs about the similarity of the administration of EpiPen and Jext no evidence had been supplied of any local confusion. The Panel, however, noted Meda's submission that it had received concerns from numerous GPs and other health professionals and that there were repeated instances of confusion whereby some prescribers believed EpiPen and Jext could be used in the same way. None of the various PCT documents were from the complainant's PCT. The identity of the complainant had not been disclosed to Meda. The company would know which PCTs had been sent the email in question. The Panel did not know what information the complainant's PCT had distributed regarding the change to Jext. The complaint was about the email from Meda and in that regard the Panel noted that it stated 'that there were no data to show what might happen if a "place and push…

design of [adrenaline auto-injector] is administered in the manner of an EpiPen…'.

It appeared from Meda's own submission that one local GP had been concerned. This was inconsistent with the email which stated 'Local GPs have suggested for us to contact you to discuss this'. There was no evidence before the Panel to indicate that there were many local clinicians who had been led to believe that there was no difference in the administration method as stated in the email or that there was local confusion. The Panel considered that the email was misleading in this regard and the statement had not been substantiated thus the Panel ruled breaches of Clauses 7.2 and 7.4. This ruling was appealed by Meda.

The Panel noted that the Code required that, *et al*, email must not be used for promotional purposes, except with the prior permission of the recipient. No such permission had been granted by the complainant who referred to the email as 'uninvited' and a breach of Clause 9.9 was ruled as acknowledged by Meda. This ruling was not appealed.

During the consideration of this case the Panel noted Meda's comment about previous cases Case AUTH/2405/5/11 and AUTH/2462/12/11. Both cases had been ruled not to be in breach of the Code and neither had been appealed by Meda (the complainant in both cases). A further letter setting out Meda's concerns had not been processed as the requirements of the Constitution and Procedure had not been met and it had not been submitted as a complaint.

The Panel was also concerned that a promotional email had been sent which had not been certified nor was prescribing information provided. It requested that Meda be advised of its concerns.

APPEAL BY MEDA

Meda remained extremely concerned that the Panel appeared not to have grasped the essential point of its message, which was to share the concerns of health professionals with their local/regional colleagues whose role was to advise on prescribing. The latter group had the influence and position to ensure clear and accurate information was provided to prescribers (and those involved in procurement) that adrenaline auto-injectors were not alike and must be used according to their licensed instructions. Meda remained concerned that this had not happened, possibly due to incorrect information from other companies.

In support of this view, Meda had already shown how a PCT and other NHS organisations had sent prescribers factually incorrect information. This had unknown consequences and it was this that Meda was attempting to address. Subsequent communication with the NHS organisations concerned had resulted in them understanding their mistakes and issuing corrected information to prescribers. However, Meda was sure the Appeal Board would agree it was preferable for this situation to be avoided.

Meda submitted that it had previously complained that ALK-Abelló's promotional and education material had inaccurately described how to administer Jext but the Panel twice ruled no breach of the Code (Cases AUTH/2462/12/11 and AUTH/2405/5/11). Meda did not appeal these rulings as it considered that it was unable to present this information any more clearly. If the Panel did not agree that correct instructions for use were vital to prescribers and users, then Meda was forced to accept this. However, Meda would not accept the perpetuation of this false information. For example, a prescriber had recently told Meda that a patient experienced bounce back from their thigh after they administered a different device in the manner of an EpiPen auto-injector, resulting in a failure to inject adrenaline. Meda submitted this was further evidence of a failure to provide prescribers with the correct information. Meda was actively following this up with the prescriber.

Meda hoped the PMCPA now appreciated the importance of this matter and that Meda was supported in future for taking a responsible approach to correcting such factual errors, whether published by the NHS or any other organisation. If such efforts were discouraged by the PMCPA, it would be extremely concerning for the pharmaceutical industry. Meda was encouraged that it took the correct action by the fact that five of the seven recipients of the email requested a meeting to discuss the points raised, whereas only one recipient had complained.

Meda submitted that the Panel appeared at first to appreciate the points raised in the message, stating that it considered it extremely important that adrenaline auto-injectors were used according to the instructions in the SPC. Although the Panel also appeared to appreciate the significance of the factually incorrect information issued by a number of NHS organisations it concluded that no such incorrect written information was issued by the complainant's PCT and therefore Meda's concerns and those of the GPs involved were not valid. This was confusing. The lack of written guidance from the complainant's PCT did not invalidate the concern, nor prove its absence in the relevant area. Meda's provision of material from various NHS organisations was intended to illustrate the point to the Panel, rather than prove its validity in a specific geographical area. Similarly, the number of GPs expressing concerns appeared to have influenced the ruling, whereas Meda submitted that even a single GP with concerns should be listened to and supported. Concerns were raised in the territories of all recipients of the email. Meda therefore strongly disputed that the email was misleading or unsubstantiated and therefore denied a breach of Clauses 7.2 and 7.4.

Meda was also keen to understand who was culpable if a patient was harmed because they failed to receive treatment due to receipt of inaccurate

information. Meda was committed to ensuring this did not happen and would continue to support its customers accordingly.

RESPONSE FROM THE COMPLAINANT

The complainant stated that he agreed with the Panel's rulings.

APPEAL BOARD RULING

The Appeal Board considered it was extremely important that adrenaline auto-injectors were used in accordance with their SPCs. It was also important that activities and materials complied with the Code.

The email at issue stated that 'Local GPs have suggested [that Meda] contact you to discuss [confusion regarding the mechanism of administration for different adrenaline auto-injectors]'. The complainant submitted that his local PCT had not received any reports of concerns from GPs. In its response Meda submitted that the email was sent to the complainant on the recommendation of a local health professional. The Panel had thus considered that the reference in the email to 'Local GPs' was misleading and could not be substantiated. Breaches of Clauses 7.2 and 7.4 were ruled.

The Appeal Board considered that Meda's submissions had been confusing and inconsistent but it noted that at the appeal further and better particulars had been produced. In that regard the Appeal Board noted that it had found it particularly helpful that the author of the email attended the appeal. The identity of the complainant had not been disclosed to Meda nor had the name of the relevant PCT. The Appeal Board considered that Meda had produced in its written and oral submissions, evidence to show that many GPs did not clearly understand the difference in the way that the various auto-injectors (notably EpiPen and Jext) should be administered. The Meda representatives stated that over forty GPs and pharmacists had expressed concern in this regard and between twelve and fifteen had asked the author of the email to write to PCTs about the matter. Taking all the circumstances into account the Appeal Board did not consider that the email was misleading on this point. No breach of Clause 7.2 was ruled. In the Appeal Board's view the claim had been substantiated. No breach of Clause 7.4 was ruled. The appeal on both points was successful

Complaint received **9 March 2012**

Case completed **28 June 2012**

CASE AUTH/2490/3/12

VOLUNTARY ADMISSION BY BAYER HEALTHCARE

Conduct of an employee

Bayer Healthcare voluntarily admitted that a healthcare development consultant (HDC) had prepared and used three documents which related to Xarelto (rivaroxaban) without the company's knowledge or approval. In accordance with Paragraph 5.6 of the Authority's Constitution and Procedure, the Director treated the matter as a complaint. Xarelto was a non-vitamin K antagonist oral anticoagulant.

Bayer stated that a service improvement manager for an NHS heart and stroke network had written to the company outlining a number of concerns about a proposal for joint working she had received from the HDC. Bayer submitted that the documents given by the HDC to the service improvement manager raised a number of very serious concerns about the proposal, namely; it was promotional; the 'costs and claims' were not 'accurate and approved by Bayer'; the 'comparative claims' were not 'accurate, fair and based on data'; reference was made to 'future indications' and 'out of licence claims'; it did not comply with the Code and guidance for joint working. In view of the above, Bayer admitted multiple breaches of the Code.

Bayer submitted that the subsequent investigation revealed that the HDC had worked on two projects. The first was with the medicines management team to help develop a business case for rivaroxaban to be included on the formulary for the primary care trust (PCT). The second project was with the service improvement manager on the development of a patient access pathway for the introduction of the new non-vitamin K antagonist oral anticoagulants. The HDC sent the service improvement manager a copy of the business case for information along with the project initiation document and the draft patient access pathway. It was the content of these documents that prompted the service improvement manager to complain to Bayer. The three documents were developed and distributed entirely at the HDC's own initiative and unbeknown to Bayer; they were not submitted for review and certification.

The detailed response from Bayer is given below.

The Panel noted that other than the documents at issue and a copy of the Xarelto 15mg summary of product characteristics (SPC) Bayer had not supplied copies of any references in support of its admissions. The Panel thus relied upon Bayer's admissions when it made its rulings.

The Panel noted that none of the documents at issue had been approved for use by Bayer; they had been developed and distributed entirely on the initiative of the HDC. The Panel noted, however, that a previous draft of the rivaroxaban business case was first seen by the HDC's line manager (a regional business manager (RBM)) in October 2011. The document was further discussed in January 2012 at a sales meeting. On the first occasion the HDC was reminded by the RBM about the need for the document to be approved and on the second occasion the national sales manager stressed the need for certification to both the RBM and the HDC. There was no follow-up on either occasion from the RBM to check that the necessary action had been taken. In the Panel's view this was wholly unacceptable particularly given the discussion of the document in January 2012 – three months after the RBM had first reminded the HDC about the need for approval.

The Panel noted that a service improvement manager had been sent a package of information to support the introduction and use of rivaroxaban. The Panel considered that the documents had thus all been sent to promote the prescription of rivaroxaban and were promotional in nature. The documents had not been certified and a breach of the Code was ruled. It was not clear that Bayer had originated the documents and in that regard the Panel considered that they were disguised promotion and ruled a breach of the Code. The documents contained no prescribing information, no reference to adverse event reporting and no inverted black triangle. Breaches of the Code were ruled. All of the above breaches of the Code were acknowledged by Bayer.

The Panel noted that the rivaroxaban business case contained many statements that were misleading with regard to the licensed indication for the medicine, the requirement for patient monitoring, interactions with food and/or concomitant medicines, the safety and cost effectiveness of rivaroxaban. Breaches of the Code were ruled. The Panel further noted that the business case also contained a number of hanging comparisons and statements that could not be substantiated. Breaches of the Code were ruled. Misleading comparisons of rivaroxaban with competitor medicines were made. Breaches of the Code were ruled. In addition, reference was made to a future indication for rivaroxaban. A breach of the Code was ruled. All of the above breaches of the Code were acknowledged by Bayer.

The Panel noted that the project initiation document, which appeared to be a joint working proposal, set out a pilot patient access pathway for the introduction of a non-vitamin K antagonist oral anticoagulant (rivaroxaban). External support for one day a week would be provided to support the project. The Panel considered that the proposal was in effect an inducement to prescribe rivaroxaban. The Panel considered that the document was

unbalanced and a breach of the Code was ruled as acknowledged by Bayer.

The Panel noted that the draft patient pathway referred to arterial fibrillation, not atrial fibrillation. The Panel also noted Bayer's submission that the pathway was not accurate and was misleading. The Panel ruled a breach of the Code as acknowledged by Bayer.

The Panel noted that the documents at issue were very poor quality and had been produced outside of the company's approval process and circulated to a number of health professionals by the HDC. A breach of the Code was ruled with regard to the failure of the HDC to maintain high standards. The Panel noted its rulings above and its concerns with regard to the poor management of the HDC. In that regard the Panel considered that the company had not maintained high standards and a breach of the Code was ruled.

The Panel considered that the circulation, albeit limited, of such poor quality documents which contained multiple errors, including misleading statements with regard to patient safety, was such as to bring discredit upon or reduce confidence in the pharmaceutical industry. The Panel ruled a breach of Clause 2.

Bayer Healthcare voluntarily admitted that a Healthcare Development Consultant (HDC) (employed on contract through a third party) had prepared and used three documents which related to Xarelto (rivaroxaban) without the company's knowledge or approval. In accordance with Paragraph 5.6 of the Authority's Constitution and Procedure, the Director treated the matter as a complaint.

Xarelto was a non-vitamin K antagonist oral anticoagulant.

COMPLAINT

Bayer stated that in February 2012, it received a letter from a service improvement manager for an NHS heart and stroke network (a clinical network hosted by the NHS) which outlined a number of concerns about a proposal for joint working. The service improvement manager referred to the following three documents which had been given to her by the HDC:

- project initiation document: a pilot for a patient access pathway
- draft patient access pathway for atrial fibrillation (AF)
- rivaroxaban business case.

Bayer provided copies of the documents and submitted that they raised a number of very serious concerns about the proposal, namely:

- It was promotional; it should not 'point a pathway in favour of pharmaceutical products or be contingent on formulary inclusion'.
- The 'costs and claims' were not 'accurate and approved by Bayer'.
- The 'comparative claims' were not 'accurate, fair and based on data'.
- Reference to 'future indications' and 'out of licence claims'.
- It did not comply with the Code and guidance for joint working.

In view of the above, Bayer admitted breaches of Clauses 3.1, 4.1, 4.10, 4.11, 7.2, 7.3, 12.1, 14.1, 15.2 and 9.1.

Bayer submitted that the subsequent investigation revealed that the HDC had worked on two projects. The first was with the medicines management team to help develop a business case for rivaroxaban to be included on the formulary for the primary care trust (PCT). The rivaroxaban business case was sent to two members of the medicines management team, a formulary development pharmacist and a GP who sat on the formulary advisory board.

The second project was with the service improvement manager on the development of a patient access pathway for the introduction of the new non-vitamin K antagonist oral anticoagulants. The HDC had a good working relationship with the service improvement manager and sent her a copy of the business case for her information along with the project initiation document and the draft patient access pathway. It was the content of these documents that prompted the service improvement manager to complain to Bayer. The three documents were developed and distributed entirely at the HDC's own initiative and unbeknown to Bayer; they were not submitted for review and certification.

Bayer submitted that the review and approval process for marketing and educational materials/activities was defined by a Bayer standard operating procedure (SOP) which clearly stated that all promotional items, non-promotional items and proposals for activities must be certified according to the Code.

Bayer had trained and validated the HDC on the requirements of the Code and the company's relevant SOPs. Bayer provided details of the HDC's ABPI Medical Representatives Examination status. Bayer submitted that despite the appropriate training, the HDC initiated and distributed the unapproved documents with disregard for the requirements of the Code, the ABPI guidance on joint working and Bayer internal policies.

As a result the HDC was immediately suspended and subsequently his/her contract was terminated. In addition Bayer noted that it had had a face-to-face meeting with the service improvement manager in March 2012 to address her concerns and to give a full and accurate account of the events together with the subsequent actions. At the meeting Bayer emphasised that it took this matter seriously and that a voluntary admission would be made to the PMCPA.

The service improvement manager stated that, despite this regrettable incident, she was still keen to enter into joint working with Bayer.

Bayer regarded the HCD's failure to apply his/her training and follow company procedures designed to ensure compliance with the Code, as a serious matter, hence its voluntary admission. Bayer trusted that the Authority would regard the actions that it had taken to address, what it believed to be, an isolated incident as satisfactory.

The Authority wrote to Bayer seeking further information and asked for its comments in relation to Clause 2 of the Code in addition to those clauses referred to above.

RESPONSE

Bayer's concerns with regard to the HDC's activities in terms of Clause 2 were mainly related to the unlicensed indications mentioned in the business case document, and therefore patient safety. However, there was never any question that this joint working project, in the early draft form proposed by the HDC, would have gone ahead. The national sales manager knew of the proposed project and was acutely aware that joint working projects and all associated documents had to be certified in accordance with Bayer SOPs on certification and joint working. These SOPs were designed to ensure compliance with the Code, the ABPI Guidance Notes on Joint Working between Pharmaceutical Companies and the NHS and Others for the Benefit of Patients and the Department of Health 'NHS Best Practice Guidance on Joint Working'.

Bayer considered that its actions to address this matter, together with its voluntary admission, were sufficient testimonial to its compliance culture as well as commitment to self-regulation and that therefore it had not brought the industry into disrepute.

Bayer explained that the HDC and the service improvement manager had discussed a proposal for a patient access pathway to help with the introduction and prescribing of non-vitamin K antagonist anticoagulants. In these preliminary discussions the HDC developed and used the project initiation document in conjunction with the draft patient access pathway for atrial fibrillation, on which the pilot patient access pathway was outlined. The documents were used for preliminary discussions around the project and apparently the HDC intended to get them certified once both parties had agreed the details of the project. The HDC therefore fundamentally misunderstood the certification requirements of the Code.

At the same time the HDC had also discussed a formulary application with the medicines management team at this particular trust. The HDC had developed the uncertified rivaroxaban business case document to use in these discussions to outline the rationale for Xarelto to be included on the trust formulary.

The HDC sent to the service improvement manager, for her feedback and comment, the project initiation and patient access documents which had been used in their discussions. The rivaroxaban business case was, in the words of the HDC, 'sent in what I believed to be the interests of transparency'; he/she thought it might be useful background information.

The HDC sent all three documents to two members of the medicines management team, a formulary development pharmacist and a GP who sat on the formulary advisory board.

It was subsequently discovered that the HDC had emailed copies of the rivaroxaban business case to three other HDCs. Bayer stated that they had not discussed or distributed these documents either internally or externally, and the electronic copies had been destroyed.

Bayer submitted that none of the three documents had been certified, in breach of Clause 14.1, and none contained the required prescribing information, adverse event reporting statement or black triangle in breach of Clauses 4.1, 4.10 and 4.11 respectively.

Bayer submitted that the documents were disguised promotion in breach of Clause 12.1.

With regard to the content of the rivaroxaban business case document, Bayer noted the following:

- 'Prevention of DVT [deep vein thrombosis] post hip or knee replacement surgery in adults', or similar.

This was not accurate in breach of Clause 7.2. The correct statement would be 'prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery'.

- 'The use of Rivaroxaban in AF [atrial fibrillation] patients for the prevention of stroke'.

This was not accurate and was misleading in breach of Clause 7.2. The correct statement should be 'Prevention of stroke and systemic embolism in eligible adult patients with non-valvular atrial fibrillation'.

- 'Both Warfarin and LMWH [low molecular weight heparin] may well be affected by compliance, concordance and side effect issues thus reducing the clinical effectiveness of the management regimen.'

Although it was true that compliance, concordance and side effects could be an issue with these medicines Bayer could not substantiate the claim that clinical effectiveness was reduced as a result. This was also unbalanced as it did not mention any issues which might arise with the use of rivaroxaban. Therefore this statement was in breach of Clauses 7.2 and 7.4.

- 'Rivaroxaban is an oral once daily anticoagulant (direct Factor Xa inhibitor) having a fixed dose regime, requires no monitoring, has low drug-drug interactions and an improved safety profile'.

Bayer submitted that this was not accurate and was misleading as it implied that patients on rivaroxaban required no monitoring whereas they would need to be monitored in a general sense. What should have been stated was 'no routine anticoagulation monitoring'. This statement also contained a hanging comparison as it referred to an improved safety profile but did not state in comparison to what. Therefore this statement was in breach of Clause 7.2.

- 'No Monitoring: reducing direct and indirect cost and resource pressure on Warfarin clinics and patients. Thus releasing capacity'.

Bayer submitted that it was not acceptable to say 'no monitoring' for the reasons outlined above. As this statement stood it was not sufficiently complete and would require further quantification, it was therefore in breach of Clause 7.2.

- 'Response profile is not influenced by diet, concomitant medications, age or ethnicity'.

Bayer stated that this was not accurate and was misleading as both the 15mg and 20mg doses had to be taken with food, it was only the 10mg dose that did not need to be taken with food. Also rivaroxaban was potentially influenced by concomitant medicines. Therefore this statement was in breach of Clause 7.2.

- 'Greater patient empowerment'

Bayer submitted that this statement was not capable of substantiation and therefore in breach of Clause 7.4.

- All of the the statements under the heading 'Outline benefits to:'

Bayer submitted that these were hanging comparisons. The statement 'Reduced risk of significant event owing to reductions in TTR' [time in therapeutic range] could not be substantiated. All the statements under the sub-heading 'Local Health Economy' were also hanging comparisons and were not capable of substantiation. Bayer therefore submitted that these sections were in breach of Clauses 7.2 and 7.4.

- 'Management of this "at greater risk population" will reduce the burden on the local healthcare economy in both direct and indirect social care/economic impact costs associated with TIA, [transient ischaemic attack] Stroke, DVT, PE [pulmonary embolism] and AF'.

Bayer submitted that this statement could not be substantiated and was in breach of Clause 7.4.

- 'Rivaroxaban shows superiority over enoxaparin a convenient administrative schedule (following epidural) and clinical use (mild/moderate renal impairment)'

Bayer submitted that this was shown in the referenced study (Grosso and Bodalia 2009) however it was unbalanced and therefore in breach of Clause 7.2. To provide a balanced overview more information should have been included. Quotations from the study included:

> 'The dosing schedule for rivaroxaban is more simple than that of dabigatran and is more appropriate for patients undergoing surgery with an epidural.'
>
> 'Since rivaroxaban also appears more convenient in both its administrative schedule (following epidural) and clinical use (in mild/ moderate renal impairment), the University College London Hospitals NHS Foundation Trust Use of Medicines Committee approved the use of rivaroxaban in place of LMWH for extended thromboprophylaxis after THR [total hip replacement] and TKR [total knee replacement] surgery.'
>
> 'Rivaroxaban has an advantage over dabigatran since it can be used in patients with a creatinine clearance of 15–30ml/minute (with caution, based on limited clinical data).'

- 'Intracranial and fatal bleeding occurred less frequently in the Rivaroxaban group'.

Bayer stated that although this statement was true and could be substantiated it did not provide a balanced overview of the data, it was misleading and a hanging comparison in breach of Clause 7.2. It should have been stated that there were more gastrointestinal (GI) bleeds in the rivaroxaban group compared with warfarin.

- This section included information on potential future indications for rivaroxaban (prevention of thromboembolic events in patients with acute coronary syndrome and treatment of symptomatic pulmonary embolism), and was therefore in breach of Clause 3.1. This information appeared in Section 1.5 and the table in Section 2.7.

- 'In patients with recent acute coronary syndrome, rivaroxaban reduced the risk of the composite endpoint of death from cardiovascular causes, myocardial infarction or stroke'

Bayer submitted that this statement was true, but only part of the quotation from the referenced study (Husten 2011) was used. The quotation from Husten also stated: 'Rivaroxaban increased the risk of major bleeding and intracranial hemorrhage but not the risk of fatal bleeding'. By leaving out the second sentence it was misleading and not balanced and therefore in breach of Clause 7.2.

- 'Rivaroxaban requires no monitoring or dose adjustments'.

Bayer stated that the statement regarding dose adjustments was true for the prevention of VTE in adult patients undergoing elective hip or knee replacement surgery (10mg dose). However, for the prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation and for the treatment of DVT, and prevention of recurrent DVT and pulmonary embolism (PE) following an acute DVT in adults, the claim was misleading and not accurate, as dose adjustments were required for renally impaired patients. Bayer also referred to its comments above about monitoring. This statement was therefore in breach of Clause 7.2.

- 'Rivaroxaban has been demonstrated to be cost effective in a number of studies across the orthopaedic indication dominating enoxaparin including in the UK setting using life LYs and QALYs [quality adjusted life years] as measures'

Bayer stated that this statement did not accurately reflect the references (McCullagh *et al* 2009 and Hamidi *et al* 2011) and was therefore in breach of Clause 7.2. McCullagh *et al* actually stated: 'Base-case analysis indicates that when both rivaroxaban and dabigatran etexilate are compared with enoxaparin sodium, rivaroxaban is the less costly and more effective option after THR and TKR. Probabilistic sensitivity analysis indicates that rivaroxaban is the most cost-effective strategy at a cost-effectiveness threshold of €45,000 per QALY; however, there is uncertainty regarding this strategy being more cost effective than dabigatran etexilate when both are compared with enoxaparin sodium'.

- 'Dabigatran has been reported to be associated with a higher risk of acute coronary events'.

Bayer submitted that this was a hanging comparison and required further quantification and explanation, and was therefore in breach of Clause 7.2.

- The table comparing rivaroxaban with dabigatran.

Bayer submitted that the table contained incomplete information and was therefore unbalanced and misleading in breach of Clauses 7.2 and 7.3. The following information should have been presented:

Class, Posology & Administration: For the prevention of stroke and systemic embolism the recommended dose is 20mg once daily, which is also the recommended maximum dose. The recommended dose for the initial treatment of acute DVT is 15mg twice daily for the first three weeks followed by 20mg once daily for the continued treatment and prevention of recurrent DVT and PE.

Renal impairment: No dose adjustment is necessary in patients with mild renal impairment (creatinine clearance 50-80ml/min). In patients with moderate (creatinine clearance 30-49ml/min) or severe (creatinine clearance 15-29ml/min) renal impairment the following dosage recommendations apply:

- For the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation, the recommended dose is 15mg once daily.

- For the treatment of DVT and prevention of recurrent DVT and PE: Patients should be treated with 15mg twice daily for the first 3 weeks. Thereafter, the recommended dose is 15mg once daily based on pharmacokinetic modeling.

Limited clinical data for patients with severe renal impairment (creatinine clearance 15-29ml/min) indicate that rivaroxaban plasma concentrations are significantly increased therefore, Xarelto is to be used with caution in these patients. Use is not recommended in patients with creatinine clearance < 15ml/min.'

Bayer further noted that the section entitled 'Key Drug-Drug interactions/cautions' had been left blank for rivaroxaban which was misleading as it implied there were no interactions with other medicines or cautions.

Bayer also submitted that the section of the table entitled 'Licence indications CHMP [Committee for Medicinal Products for Human Use] and/or NICE [National Institute for Health and Clinical Excellence] approval' was not clear and was ambiguous about which indication was CHMP approved and which had NICE approval. Rivaroxaban was recommended by NICE for the orthopaedic indication but not for the prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation or the treatment of DVT, and prevention of recurrent DVT and pulmonary embolism (PE) following an acute DVT in adults.

Turing to the project initiation document, Bayer submitted that it was unbalanced as it referred only to the use of rivaroxaban, whereas this type of project should include all available therapeutic options for this patient group. The document was therefore in breach of Clause 7.2.

Bayer noted that the draft patient access pathway referred to 'Arterial Fibrillation' which was not accurate; it was 'Atrial Fibrillation'. In addition the flow was not accurate and was misleading, and therefore in breach of Clause 7.2.

Bayer explained that the HDC's line manager (regional business manager (RBM)) was the first person to see the rivaroxaban business case in October 2011. That version was an earlier draft of the document received by the service improvement manager. The RBM did not see the project initiation or the patient access documents until after the service improvement manager had complained.

No one else at Bayer saw the documents until after the complaint had been made by the service improvement manager.

Bayer submitted that when the RBM first saw the rivaroxaban business case in October 2011 he expressed concerns and asked the HDC if it had been submitted for approval. The RBM was assured by the HDC that it was 'under medical review'. The RBM did not check to see if this was the case. Bayer noted that the rivaroxaban business case was never submitted for approval.

Bayer stated that the rivaroxaban business case was discussed at a sales meeting on 9 January 2012. The national sales manager (the RBM's line manager) stressed to both the HDC and the RBM that that document and any others associated with it would have to be certified as soon as possible, and specifically before the project went any further. However no specific actions, follow-up or timelines were put in place to ensure that this was done. Nevertheless the HDC role was a senior one and ordinarily these individuals should not require such close supervision.

Bayer stated that its SOP on the internal process for the initiation and conduct of a joint working project clearly stated that all materials and activities associated with joint working must be certified in accordance with its certification process (ie all promotional items, non-promotional items and proposals for activities must be certified according to the Code).

Bayer submitted that in terms of formulary applications there was no set process as it was a sales process and would differ slightly in every health economy in the UK. Trusts and PCTs often produced their own guidelines for formulary applications, and in these cases the guidance was strictly followed. However the consistent principle was that the Code was followed throughout and in particular compliance with its certification process.

PANEL RULING

The Panel noted that other than the documents at issue and a copy of the Xarelto 15mg summary of product characteristics (SPC) Bayer had not supplied copies of any references in support of its admissions. The Panel thus relied upon Bayer's admissions when it made its rulings.

The Panel noted that none of the documents at issue had been approved for use by Bayer; they had been developed and distributed entirely on the initiative of the HDC. The provision of these documents had prompted a service improvement manager to complain to Bayer. It appeared that the documents had been provided to the service improvement manager in February 2012. The Panel noted, however, that a previous draft of the rivaroxaban business case was first seen by the HDC's line manager (an RBM) in October 2011. The document was further discussed in January 2012 at a sales meeting. On the first occasion the HDC was reminded by the RBM about the need for the document to be approved and on the second occasion the national sales manager stressed the need for certification to both the RBM and the HDC. There was no follow-up on either occasion from the RBM to check that the necessary action had been taken. In the Panel's view this was wholly unacceptable particularly given the discussion of the document in January 2012 – three months after the RBM had first reminded the HDC about the need for approval. The Panel noted Bayer's submission that the seniority of the HDC role suggested that close supervision was not necessary. In the Panel's view, however, the repeated internal discussion of the business case document by the HDC concerned should have alerted senior managers otherwise.

The Panel noted that a service improvement manager had been sent a package of information to support the introduction and use of rivaroxaban. The business case document stated that the aim of the document was to provide evidential support for the adoption of rivaroxaban onto the local formulary. The project initiation document stated that the project would, *et al*, provide a clear and unambiguous access pathway to rivaroxaban. The patient pathway document did not refer to rivaroxaban specifically but appeared to be an integral part of the package. The Panel considered that the documents had all been sent to promote the prescription of rivaroxaban and were thus promotional in nature. The documents had not been certified and a breach of Clause 14.1 was ruled. It was not clear that Bayer had originated the documents and in that regard the Panel considered that they were disguised promotion and ruled a breach of Clause 12.1. The documents contained no prescribing information, no reference to adverse event reporting and no inverted black triangle. The Panel ruled breaches of Clauses 4.1, 4.10 and 4.11 respectively. All of the above breaches of the Code were acknowledged by Bayer.

Turning to the content of the rivaroxaban business case, the Panel noted that there were several references to the medicine being licenced to prevent DVT post hip or knee replacement surgery. Rivaroxaban was in fact licensed to prevent VTE which included not only DVT but also pulmonary embolus. The Panel considered that the claims were incorrect as acknowledged by Bayer. A breach of Clause 7.2 was ruled.

Page one of the business case referred to 'The use of Rivaroxaban in AF patients for the prevention of stroke'. The Panel noted that rivaroxaban was licensed for the prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors. The Panel thus considered that the statement in the business case document was inaccurate and misleading. A breach of Clause 7.2 was ruled as acknowledged by Bayer.

The Panel noted Bayer's submission that the statement that 'Both Warfarin and LMWH may well be affected by compliance, concordance and side effect issues thus reducing the clinical effectiveness

of the management regimen' could not be substantiated and that there was no comparable reference to issues which might arise with rivaroxaban. The Panel thus considered that the statement was unbalanced and unsubstantiable. Breaches of Clauses 7.2 and 7.4 were ruled as acknowledged by Bayer.

The Panel noted that the business case stated that rivaroxaban required no monitoring; it was unclear as to what that meant. The SPC stated that clinical surveillance in line with anticoagulation practice was recommended throughout the treatment period and Bayer had submitted that patients would have to be monitored in the general sense. The Panel considered that references to 'no monitoring' were thus misleading as acknowledged by Bayer. A breach of Clause 7.2 was ruled.

The Panel noted the claim that 'Rivaroxaban….has… .an improved safety profile'. It was not stated that with which the medicine was compared. The claim was thus a hanging comparison as acknowledged by Bayer and the Panel ruled a breach of Clause 7.2.

The Panel noted that the business case stated that the response profile of rivaroxaban was not influenced by, *et al*, diet and/or concomitant medications. This was not so. Doses of rivaroxaban above 10mg had to be taken with food in order to increase its bioavailability. Further, Section 4.5 of the Xarelto 15mg SPC, interaction with other medicinal products and other forms of interaction, stated that co-administration of some medicines (eg ketoconazole or ritonavir) would increase the bioavailabilty of rivaroxaban whilst the co-administration of others (eg rifampicin) would decrease its bioavailability. The Panel considered that the claim at issue was inaccurate and misleading as acknowledged by Bayer. A breach of Clause 7.2 was ruled.

The business case document stated that one of the benefits of treatment for the patient was 'Greater patient empowerment'. The Panel noted Bayer's submission that this claim could not be substantiated. A breach of Clause 7.4 was ruled.

The Panel noted that Section 1.4 of the business case document contained the following hanging comparisons; 'Greater patient empowerment'; 'Better care…'; 'Fewer admission…'; '…fewer medicine related adverse events….; '…better medicines management' and 'Better use of resources…'. The Panel ruled a breach of Clause 7.2 in each case as acknowledged by Bayer. The same section of the document also contained the statement 'Reduced risk of significant event owing to reductions in TTR [time in therapeutic range]' which Bayer had submitted could not be substantiated. The company had also submitted that the four statements under the heading 'Local Health Economy' could not be substantiated. The Panel thus ruled each statement in breach of Clause 7.4.

The Panel noted Bayer's submission that the statement 'Management of this "at greater risk population" will reduce the burden on the local healthcare economy in both direct and indirect social care/economic impact costs associated with TIA, Stroke, DVT, PE and AF' could not be substantiated. The Panel thus ruled a breach of Clause 7.4.

The Panel noted Bayer's submission that the claim 'Rivaroxaban shows superiority over enoxaparin a convenient administrative schedule (following epidural) and clinical use (mild/moderate renal impairment)' was unbalanced in breach of Clause 7.2. The claim was referenced to Grosso and Bodalia which was a study of dabigatran vs rivaroxaban for thromboprophylaxis. It was not a comparison of rivaroxaban and enoxaparin as implied by the claim. The Panel considered that the claim was thus misleading. A breach of Clause 7.2 was ruled.

The Panel noted that beneath a heading of 'Rivaroxaban versus Warfarin in Non-Valvular Atrial Fibrillation' was the claim 'Intracranial and fatal bleeding occurred less frequently in the Rivaroxaban group'. Bayer had submitted that this claim was a hanging comparison but the Panel considered that, given the heading, it was clear as to with what rivaroxaban was compared. No breach of Clause 7.2 was ruled in that regard. The Panel further noted Bayer's submission that there were more GI bleeds in the rivaroxaban group compared with the warfarin group. Given the reference to bleeding risk the Panel considered that it was misleading and unbalanced to refer to the favourable results for intracranial and fatal bleeding but not to the unfavourable results for GI bleeding. A breach of Clause 7.2 was ruled.

The Panel noted that the business case document referred to future indications for rivaroxaban, ie acute coronary syndrome. Rivaroxaban did not have a marketing authorization for acute coronary syndrome and so in that regard the Panel ruled a breach of Clause 3.1 as acknowledged by Bayer. The Panel further noted Bayer's submission that the claim 'In patients with recent acute coronary syndrome, rivaroxaban reduced the risk of the composite endpoint of death from cardiovascular causes, myocardial infarction or stroke' was referenced to Mega *et al* (2011). The Panel noted Bayer's submission that this was misleading in breach of Clause 7.2 as it did not refer to the increased risk with rivaroxaban of major bleeding and intracranial hemorrhage also seen in this study. The Panel considered that the claim was misleading as acknowledged by Bayer; a breach of Clause 7.2 was ruled.

The business case document contained the claim 'Rivaroxaban requires no monitoring or dose adjustments'. The Panel noted that this was not so for all patients, eg Section 4.2 of the Xarelto 15mg SPC, Posology and method of administration, stated that for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation, the daily dose of rivaroxaban should be decreased from 20mg to 15mg in those with moderate to severe renal impairment. In addition the Panel noted its comments and rulings about in relation to references to no monitoring. The Panel

considered that the claim was misleading as acknowledged by Bayer. A breach of Clause 7.2 was ruled.

The Panel noted Bayer's submission that the claim 'Rivaroxaban has been demonstrated to be cost effective in a number of studies across the orthopaedic indication dominating enoxaparin including in the UK setting using life LYs and QALYs as measures' was not accurate; it appeared that one of the references cited in support of the claim (McCullagh *et al*) was more equivocal in its conclusion. A breach of Clause 7.2 was ruled.

The Panel noted that the business case contained the claim 'Dabigatran has been reported to be associated with a higher risk of acute coronary events'. Dabigatran was a competitor product to rivaroxaban (marketed by Boehringer Ingelheim). The Panel considered that within the context of a business case document for rivaroxaban, it would be clear that dabigatran was being compared with rivaroxaban. In that regard the Panel did not consider that the claim was a hanging comparison as stated by Bayer and no breach of Clause 7.2 was ruled.

The Panel noted Bayer's submission that there were multiple omissions in a table of data comparing rivaroxaban with dabigatran. The Panel noted that the data regarding class, posology and administration was incomplete; the data on renal impairment was limited and there was no data at all given for rivaroxaban with regard to key drug-drug interactions/cautions. The information stated with regard to which indications had been approved by NICE was ambiguous. The Panel considered overall that the table of data and the comparisons within were misleading. Breaches of Clause 7.2 and 7.3 were ruled.

The Panel noted that the project initiation document, which appeared to be a joint working proposal, set out a pilot patient access pathway for the introduction of a non-vitamin K antagonist oral anticoagulant (rivaroxaban). External support for one day a week would be provided to support the project. The Panel considered that the proposal was in effect an inducement to prescribe rivaroxaban although there were other oral anticoagulants in the same class. Given the lack of reference to the other medicines in the same class the Panel considered that the document was unbalanced and a breach of Clause 7.2 was ruled as acknowledged by Bayer.

The Panel noted that the draft patient pathway referred to arterial fibrillation, not atrial fibrillation. The Panel also noted Bayer's submission that the pathway was not accurate and was misleading. The Panel ruled a breach of Clause 7.2 as acknowledged by Bayer.

The Panel noted that the documents at issue were very poor quality and had been produced outside of the company's approval process and circulated to a number of health professionals by the HDC. A breach of Clause 15.2 was ruled with regard to the failure of the HDC to maintain high standards. The Panel noted its rulings above and its concerns with regard to the poor management of the HDC. In that regard the Panel considered that the company had not maintained high standards and a breach of Clause 9.1 was ruled.

The Panel considered that the circulation, albeit limited, of such poor quality documents which contained multiple errors, including misleading statements with regard to patient safety, was such as to bring discredit upon or reduce confidence in the pharmaceutical industry. The Panel ruled a breach of Clause 2.

Complaint received **14 March 2012**

Case completed **25 May 2012**

CASE AUTH/2492/3/12

PRESCRIBING ADVISOR v MEDA

EpiPen booklet

A prescribing advisor complained about the tone and content of a booklet entitled 'The Case for EpiPen (Adrenaline) Auto-Injector' which he had received from Meda Pharmaceuticals. In the complainant's view the document was sensationalist, emotive and unsubstantiated. Overall, the complainant considered that the booklet was unprofessional and sought to create alarm rather than provide a rational, proportionate response to a competitor product.

The detailed response from Meda is given below.

The complainant objected to the claim 'Moving away from EpiPen Auto-Injector to an alternative auto injector brand should be carefully considered on a regional level...' as he considered it was reasonable, and in fact now being encouraged, to make decisions at a local level.

The Panel disagreed with Meda's submission that there was no difference between 'regional' and 'local' in this context. The Panel noted that the booklet appeared to use 'regional' and 'PCT' interchangeably, referring to the 'PCT region' and 'region or PCT'. The booklet was distributed to PCTs and in that regard the Panel considered that the target audience would understand 'regional' to cover a much larger geographical area than that covered by a PCT. This appeared to be the complainant's understanding. The Panel considered that the use of the term 'regional' in this context was misleading; a breach of the Code was ruled.

The complainant alleged that the claim 'Many patients are likely to be unhappy with the prospect of a change from EpiPen Auto-Injector to an alternative device' was unsubstantiated conjecture.

The Panel considered that although the claim stated 'Many patients are *likely* to be unhappy…' (emphasis added), this did not negate the impression that many patients *would* be unhappy to change from EpiPen to an alternative device; there was no data to substantiate such a claim. The Panel ruled a breach of the Code. The Panel considered that in the absence of substantiating data the claim was misleading. A breach of the Code was ruled.

The complainant objected to the claims 'There would need to be a regional decision …' 'This is a massive task…' as he considered that this did not have to be done on a regional basis.

The Panel noted its comments above in relation to the term regional. The Panel considered that its ruling above applied here and ruled a breach of the Code. The Panel considered that it was likely that switching a patient's adrenaline auto injector would inevitably require retraining of patients, physician's and others. The claim in question was followed by a detailed discussion of the tasks required and a flow chart setting out a PCT implementation plan. Meda had provided no data to quantify the amount of time this would require. In that regard the Panel considered that the claim 'This is a massive task' was misleading and could not be substantiated, and breaches of the Code were ruled.

The complainant noted the claim 'The time and costs required to move patients from EpiPen Auto-Injector to Jext is a questionable use of scarce health resources…' and was not persuaded that it was Meda's role to influence the priorities of PCTs in this way.

The Panel considered that it was not unacceptable for companies to put forward an economic case as to why patients should stay on their medicines and not be switched to others. Such activities, however, had to comply with the Code. The Panel considered that the claim at issue implied that anyone who decided to change patients from EpiPen to Jext would waste NHS resources. In the Panel's view this failed to recognize the professional standing of the audience to which the booklet was directed. A breach of the Code was ruled.

A prescribing advisor complained about the tone of a 15 page, A4 booklet entitled 'The Case for EpiPen (Adrenaline) Auto-Injector' (ref UK/EPI/11/0053d) which he had received from Meda Pharmaceuticals Limited. In the complainant's view the document was sensationalist, emotive and unsubstantiated. Overall, the complainant considered that the booklet was unprofessional and sought to create alarm rather than provide a rational, proportionate response to a competitor product in a competitive market.

When writing to Meda, the Authority asked it to respond in relation to Clauses 7.2, 7.4 and 9.2 of the Code.

1 Claim 'Moving away from EpiPen Auto-Injector to an alternative auto injector brand should be carefully considered on a regional level...'.

This claim appeared in the summary section on page 3 of the booklet.

COMPLAINT

The complainant considered it was perfectly reasonable, and in fact now being encouraged, to make decisions at a local level and was likely to be done on a clinical commissioning group (CCG) basis in future.

RESPONSE

Meda stated that the booklet in question was sent to primary care trusts (PCTs) to help them understand the financial considerations of the various adrenaline auto injector brands available in the UK. Meda considered the booklet was accurate, fair and balanced in its presentation of data and information on anaphylaxis, relevant clinical guidelines and the factors that PCTs should consider when deciding which brands to select.

Meda agreed with the complainant; regional decisions were currently taken at PCT level and were likely to be taken by CCGs in the future. However, there seemed to be a simple disagreement on the definition of 'regional'. In Meda's view, there was no difference between 'regional' and 'local' in this context. Therefore, Meda stood by the recommendation that changing auto injector brand was a decision that should be taken on a regional level. This was to ensure that appropriate and consistent training was delivered and the risk of confusion and mistakes during administration were minimised.

PANEL RULING

The Panel noted that Meda agreed with the complainant's statement that regional decisions were currently taken at a local level and were likely to be taken by clinical commissioning groups in the future. The Panel disagreed with Meda's submission that there was no difference between 'regional' and 'local' in this context.

The Panel noted that the booklet appeared to use 'regional' and 'PCT' interchangeably, referring to the 'PCT region' and 'region or PCT'. There was detailed discussion of changes required at a PCT level. The claim in question had to stand alone in relation to the requirements of the Code. Context was, however, important. A subsequent paragraph on the page in question explained that the booklet considered the cost implications for the NHS serving a typical population of 100,000 (PCT/health board). Nevertheless, the booklet was distributed to PCTs and in that regard the Panel considered that the target audience would understand 'regional' to cover a much larger geographical area than that covered by a PCT. This appeared to be the understanding of the complainant. The Panel considered that the use of the term 'regional' in this context was misleading and a breach of Clause 7.2 was ruled.

2 Claim 'Many patients are likely to be unhappy with the prospect of a change from EpiPen Auto-Injector to an alternative device'.

This claim appeared on page 9 of the booklet under the heading 'Is moving to another adrenaline auto injector worthwhile?'.

COMPLAINT

The complainant alleged that this claim was unsubstantiated conjecture on the part of Meda.

RESPONSE

Meda submitted that a change in medicine for any patient was a significant event, particularly when the medicine was one that a quarter of a million patients currently carried and relied on as a potentially life-saving treatment. It was not unreasonable to assume that many patients might be concerned if they were switched to a device which was significantly different in appearance, size, colour and method of administration. Meda had experience of this with its asthma inhaler products, whereby patients sought reassurance from its medical information service regarding different devices. Similarly, reassurance was often sought when a change was made to product packaging.

Meda submitted that despite this, the claim in question was not definitive and deliberately used the words 'many patients are likely to be unhappy' to ensure the reader understood that not all patients would feel this way. The text in this section of the piece highlighted the resource considerations that management bodies should take when considering a wholesale switch between products. The specific claims made were intended merely to highlight the need to ensure that patients who were given a new product were appropriately trained. This was a responsible position to take.

PANEL RULING

The Panel noted Meda's submission that it was a reasonable assumption on its part that many patients would be unhappy if they were changed from EpiPen to an alternative auto injector. Although the claim stated 'Many patients are *likely* to be unhappy…' (emphasis added), the Panel did not consider that this negated the impression that many patients *would* be unhappy to change from EpiPen to an alternative device. There was also no data to substantiate such a claim. The Panel ruled a breach of Clause 7.4. The Panel considered that in the absence of substantiating data the claim was misleading. A breach of Clause 7.2 was ruled.

3 Claims 'There would need to be a regional decision …', 'This is a massive task…'.

These claims appeared on page 9 of the booklet and followed that at issue in point 2 above.

COMPLAINT

As mentioned in point 1 above the complainant considered that this did not have to be done on a regional basis.

RESPONSE

Meda somewhat agreed that the language used ('a massive task') could have been better chosen, but stood by the view that retraining all patients, health professionals (including GPs, practice nurses, pharmacists etc) and associated stakeholders (including care-givers such as parents, friends, teachers, school nurses, youth groups etc) was a

significant, time consuming and potentially expensive undertaking. This was especially relevant in the context of anaphylaxis, where all adrenaline auto injectors had a different method of administration and correct use of the device was critical for the successful treatment of a life-threatening condition.

PANEL RULING

The Panel noted its comments above in relation to the term regional. The Panel considered that its ruling in point 1 above applied here and ruled a breach of Clause 7.2.

The Panel noted that the complainant had not explained why the phrase 'This is a massive task' was misleading. The Panel further noted Meda's submission that it somewhat agreed that the language used ('a massive task') could have been better chosen, but stood by its view that retraining all patients, health professionals and associated stakeholders was a significant, time consuming and potentially expensive undertaking. The Panel considered that it was likely that switching a patient's adrenaline auto injector would inevitably require retraining of patients, physician's and others involved in the care of the patient. The claim in question was followed by a detailed discussion of the tasks required and a flow chart setting out a PCT implementation plan. Meda had provided no data to quantify the amount of time this would require. In that regard the Panel considered that the claim 'This is a massive task' was misleading and could not be substantiated, in breach of Clauses 7.2 and 7.4.

4 Claim 'The time and costs required to move patients from EpiPen Auto-Injector to Jext is a questionable use of scarce health resources…'.

This claim appeared on page 14 of the booklet and was the final highlighted block of text.

COMPLAINT

The complainant was not persuaded that it was Meda's role to influence the priorities of PCTs in this way.

RESPONSE

Meda considered that it had an ethical responsibility to inform existing and future customers of EpiPen Auto Injectors of the circumstances surrounding adrenaline auto injector use and how their consideration of an alternative product was likely to impact on them. This was relevant to individual health professionals and to healthcare organisations such as PCTs. Meda was very surprised to receive this complaint as pharmaceutical companies commonly put forward an economic case to key decision makers, be it nationally or regionally.

Meda disagreed that this was an unprofessional document, or that it breached Clauses 7.2, 7.4 or 9.2 the Code. It was an attempt to communicate important information about the implications of switching adrenaline auto injector devices. Recent evidence of PCT/trust communications received by Meda highlighted that there was confusion over the correct use of auto injectors and the company considered that it was important to correct this situation. Meda provided examples of documents from two PCTs about a proposed switch from EpiPen to Jext which contained serious errors about the use of Jext (such as 'Jext is a similar device and can be used exactly like an EpiPen'). This was inconsistent with the product summary of product characteristics (SPC) and potentially harmful and this matter had previously been brought to the Authority's attention.

PANEL RULING

The Panel noted the complainant's allegation that it was not Meda's role to influence the resource priorities of PCTs. The Panel considered, however, that it was not unacceptable for companies to put forward an economic case as to why patients should stay on their medicines and not be switched to an alternative. Such activities, however, had to comply with the Code.

The Panel considered that the claim at issue implied that anyone who decided to change patients from EpiPen to Jext would waste NHS resources. In the Panel's view this failed to recognize the professional standing of the audience to which the booklet was directed. A breach of Clause 9.2 was ruled.

Complaint received **22 March 2012**

Case completed **30 May 2012**

CASE AUTH/2493/3/12

GENERAL PRACTITIONER v ASTRAZENECA

Invitation to an advisory board

A general practitioner complained about an invitation to participate in an AstraZeneca advisory board. The invitation consisted of three pages which had been faxed to the complainant's practice.

The complainant noted that page 2 of the facsimile was addressed to 'All GP's' [sic] and the letter (page 1 of the facsimile) was addressed to 'Dr X'. The complainant considered that this implied that invitees had not been specifically selected for their relevant expertise. It further implied that the facsimile was sent to multiple practices, such that the number of consultants was not limited to what might be reasonably necessary for the purpose of the advisory board.

Pages 1 and 2 of the facsimile referred to a £300 honorarium but on page 3 £125 was offered. Either way, the complainant considered this could be regarded as an incentive to attend without regard for the level of expertise non-specified GPs might be able to contribute.

The detailed response from AstraZeneca is given below.

The Panel noted the complainant had provided copies of three invitations to an AstraZeneca advisory board, one addressed to 'Dear Dr X'; one to 'All GP's' [sic] and the other with no stated addressee; the latter invitation was, according to AstraZeneca, intended for the practice manager. The Panel noted that the invitation to 'Dear Dr X' stated that the objective of the meeting was to gain advice and feedback on new educational materials to help GPs more effectively diagnose bipolar disorder and how best to discuss these materials via a team of telephone-based service agents. Given the broad stated objectives the Panel noted that AstraZeneca aimed to recruit GPs from across the mental health and commissioning spectrum. The meeting objectives stated in the invitation for practice managers were similar to those above, with the additional objective of gaining advice and feedback on how the educational materials might support the practice and patients by achieving targets through increased and more accurate diagnosis. AstraZeneca also wanted to assess criteria upon which a practice manager might permit access to speak to a GP directly. The Panel noted the broad objectives of the advisory board and the aim to recruit managers from a broad spectrum of practices including those with no mental health lead.

The Panel noted that what appeared to be the covering letter referred only to the GP advisory board on 26 March. The practice manager invitation bore no addressee and did not make it at all clear that invitees had to be practice managers. The Panel noted the objectives of the advisory boards and consequently the broad selection criteria for participants. Given such broad selection criteria the Panel did not consider the use of the term 'All GPs' and 'Dear Dr X' in relation to a GP surgery was unreasonable, or that on the specific facts of this case the GP advisory board invitation implied that no selection had taken place as alleged. No breach of the Code was ruled in that regard. In relation to the practice manager invitation the Panel considered that the absence of any addressee, the failure to identify the status of consultants within the letter and the absence of any relevant covering letter gave a poor impression and implied that no specific selection of consultants had or would take place. A breach of the Code was ruled.

The Panel noted that although the educational module to be discussed at the advisory boards related to mental health, it would be made available to all GPs regardless of their expertise in that therapy area. The GP advisory board, if it had gone ahead, would have consisted of six GPs, one clinical commissioning group mental health lead, one GP that saw his own mental health patients and a mental health locality cluster lead. The practice manager advisory board, if it had gone ahead, would have consisted of five managers from practices where GPs had no special interest in mental health, three from practices where there was a mental health lead and two from practices where there was a clinical commissioning group mental health lead. In the Panel's view, the attendees at each advisory board had ultimately been selected such as to fairly represent the target audience for the educational materials under discussion. The Panel did not consider that an advisory board of nine or ten was a number greater than that reasonably necessary to achieve the objectives outlined above in the 3 hours available. No breach of the Code was ruled in that regard.

The Panel noted its comments and rulings above about the meetings' objectives and the consultants' honoraria. The Panel did not consider that the honoraria were an inducement to prescribe or recommend any medicine and consequently ruled no breach of the Code.

A general practitioner complained about an invitation which he had received from a market research company to take part in an AstraZeneca advisory board. The invitation consisted of three pages which had been faxed to the complainant's practice. The matter was taken up with AstraZeneca UK Limited.

COMPLAINT

The complainant noted that page 2 of the facsimile was addressed to 'All GP's' [sic] and the letter (page 1 of the facsimile) was addressed to 'Dr X'. The complainant considered that this implied that invitees had not been specifically selected for their relevant expertise. It further implied that the facsimile was sent to multiple practices, such that the number of consultants was not limited to what might be reasonably necessary for the purpose of the advisory board.

The complainant submitted that it was unclear how his practice had been selected, or whether specific GPs were being invited.

Pages 1 and 2 of the facsimile referred to a £300 honorarium but on page 3 it was stated that £125 was offered as a fee for attendance and contribution at the advisory board. Either way, the complainant considered this could be regarded as an incentive to attend without regard for the level of expertise non-specified GPs might be able to contribute.

As such, the complainant alleged that this activity was in breach of Clause 20.1 on the use of consultants and Clause 9.1, failing to maintain high standards.

When writing to AstraZeneca, the Authority asked it to respond in relation to Clauses 2 and 18.1 in addition to Clauses 9.1 and 20.1 cited by the complainant.

RESPONSE

AstraZeneca noted that the complaint centred around the selection and compensation of attendees invited to participate in an advisory board. Although the complaint was about an advisory board on 26 March 2012, another advisory board planned for the 29 March 2012 was relevant and there was further explanation below.

AstraZeneca submitted that it had worked with a third party to develop educational modules to help GPs better diagnose bipolar and unipolar depression. This was an important educational need because a depressed patient's first contact with the health service was his/her GP and misdiagnosis was common. The educational modules were written by an independent clinician chosen by the third party and were not product related, but were in the process of being certified according to AstraZeneca procedures. AstraZeneca intended the educational modules to be accessed electronically and to tell GPs about them via its TeleReach service - a service whereby ABPI qualified representatives telephoned general practices at allotted times to speak to either a practice manager or a relevant health professional to discuss a proposed non-promotional patient- or disease-centered offering. Many practices preferred the TeleReach representatives to speak to the practice manager to discuss the offering before allowing them to speak to a relevant health professional.

Given the need to understand how to correctly position a new educational service offering for serious mental health with a primary care audience and how to offer this with a new service team, AstraZeneca had organised advisory boards with the appropriate stakeholders. This need arose because with previous offerings in different therapy areas there had been a variance on how often the TeleReach team had had a telephone conversation with a GP with little insight as to why this variance might occur.

AstraZeneca submitted that the objective of the advisory board in question was to gain advice from GPs about the value of these non-promotional educational modules to their ongoing clinical practice and to gain clarity on the optimal way to explain these modules during a telephone conversation, with the aim of maximising the educational benefit of the modules and optimising the telephone interaction with the GP. Another objective for the advisory board was to discuss the TeleReach service and gain the GPs' advice and feedback on the service in general, how it might be best used and the type of services they would be interested in finding out about by this method. The advisory board was to last 3 hours on the evening of 26 March. There was no intended pre work but attendees were expected to be engaged and contribute advice for the majority of those 3 hours, which was reflected in the agenda.

However, on the day before receiving the complaint there was an announcement of a High Court decision that resulted in the unexpected loss of the Seroquel XL (long acting quetiapine) patent formulation in the UK, which was AstraZeneca's only promoted mental health product. Therefore any activities in development that related to the brand and the mental health therapy area were immediately stopped, and as this included the educational modules about depression it would have been inappropriate to continue with the advisory board which was thus cancelled. This decision was communicated to attendees on 22 March.

AstraZeneca stated that on 29 March 2012 another advisory board was planned with similar objectives but different attendees; GP practice managers. The intention of this advisory board was to discuss similar topics as outlined above but to gain specific advice from practice managers. This was because most of the time the TeleReach representatives had to speak to a practice manager before being allowed to speak to a health professional or they might only ever get to speak to the practice manager. This telephone conversation needed to be framed differently to that with a GP. Therefore it was appropriate to gain the advice of practice managers and their input into what they would want to know about these educational modules to ensure that AstraZeneca was able to communicate their benefit for GPs and ultimately patient care in their practice. In addition, it was important for AstraZeneca to gain advice on the TeleReach service from these important stakeholders. This advisory board, however, was also cancelled for the reasons stated above.

AstraZeneca submitted that it engaged a market research agency to recruit for both advisory boards. AstraZeneca gave the agency a written brief detailing the purpose of the advisory boards, including the criteria for the recruitment of attendees. The brief contained sufficient background to ensure that the agency understood the TeleReach service and the rationale behind why AstraZeneca produced educational modules about the correct diagnosis of depression. To give full context there was a brief synopsis of AstraZeneca's relevant medicine and how the brand strategy was relevant to the educational modules. The agency was not expected to mention the brand whilst recruiting, particularly as there would be no brand discussion in the advisory board.

AstraZeneca explained that it had asked the agency to recruit 8-10 GPs with differing experience and areas of interest for the advisory board. Due to the nature of the advice being sought in relation to the broad applicability of the educational materials and how best to deliver them through a TeleReach channel, it was not necessary to select individuals with significant clinical experience in mental health. Instead, the recruitment strategy required GPs from across the mental health therapeutic interest and commissioning spectrum; 1 or 2 GPs who were clinical commissioning group (CCG) mental health leads, 2 or 3 GPs who were the mental health leads for their GP practice and 4 or 5 GPs with no specific interest in mental health. AstraZeneca requested this participant breakdown because the educational modules would be available to all GPs and this proportion represented the likely final audience. This breakdown also met the requirements of the second objective of the advisory board; to obtain feedback about the TeleReach service in general. The final attendance list consisted of 9 GPs of which 3 had a particular interest in mental health because of responsibilities in their practice or CCG.

AstraZeneca stated that the briefing for the practice manager advisory board stated that 8-10 practice managers should attend; the practice managers should have worked in practices with GPs who occupied roles as CCG mental health leads (1 or 2), in GP practices with a mental health lead (2 or 3) and in GP practices where there was no mental health lead (4 or 5) in order to gain a broad spectrum of advice. Of the 10 practice managers due to attend the advisory board, 5 either had a mental health lead GP within the practice or one of their GPs was the CCG mental health lead.

AstraZeneca submitted that therefore during the recruitment process, GP practices were contacted not only to assess suitability of the GPs but also the practice manager, and the final attendee lists demonstrated that the agency worked within its brief. Unfortunately, as neither advisory board met, there were no outputs to share. However, AstraZeneca considered that it had demonstrated a strong rationale and robust reasoning for the choice and number of attendees in direct relation to the identified need, and it therefore refuted the alleged breach of Clause 20.1.

With regard to Clause 18.1 AstraZeneca submitted that attendees at an advisory board routinely received an honorarium for the provision of advice and feedback. AstraZeneca policy required the honorarium to reflect fair market value for the role and time spent, and it must not be used as an undue incentive to attend. As there was no intent to discuss an AstraZeneca product at the advisory board in question AstraZeneca considered that the reasonable honorarium offered could not be deemed an inducement to prescribe, supply, administer, recommend, buy or sell any medicine.

AstraZeneca stated that it made no attempt to target prescribers of any particular product; the recruiting agency was not given any criteria to recruit based on any sales or potential sales.

AstraZeneca submitted that the proposed honoraria took into account the professional standing of the two groups recruited and were based on AstraZeneca's fair market value in both cases. It was also appropriate to reimburse reasonable travel expenses incurred in attending the advisory board meeting. For GPs the honorarium was £300 and reimbursement of reasonable travel expenses. This was in line with AstraZeneca's fair market value table.

AstraZeneca had limited experience of engaging practice mangers for their services but it was initially considered that £125, with reasonable travel expenses, was an appropriate fair market value for a three hour advisory board. However the agency suggested that £150 would be more appropriate and this was to be reflected in the confirmatory invitation.

Thus AstraZeneca considered that it had demonstrated a clear rationale related to identification and calculation of a suitable fair market value honorarium, which was not an inducement to prescribe, supply, administer, recommend, buy or sell any medicine. AstraZeneca refuted the alleged breach of Clause 18.1.

AstraZeneca submitted that usually the recruiting agency initially tried to telephone GPs at their practices to establish their interest and relevant experience for an advisory board, using a company's recruitment criteria. If the GP was appropriate for the advisory board and indicated that he/she would be able to attend, the agency emailed him/her a formal invitation. This email had been reviewed and certified by AstraZeneca signatories for this purpose.

AstraZeneca stated that practice receptionists did not always let the agency talk to the GP or practice manager directly, but instead asked for details to be either faxed or emailed for them to pass onto the relevant person, with a brief explanation of what it related to. In cases where there was more than one

eligible GP in the practice, receptionists frequently asked for only one invitation and not one per GP. In such cases, the facsimile would be addressed to 'All GPs'. This scenario was routine practice for this agency as receptionists often limited access to GPs, to protect their time for patient care.

AstraZeneca submitted that as stated above, during this recruitment process, GP practices were contacted not only to assess the suitability of the GP but also the practice manager. If the agency could not speak to the practice manager then both invitations (GP and practice manager) would be faxed or emailed to the receptionist to pass onto the relevant people. The agency produced a covering letter to go with the invitation(s) to ensure the receptionist could identify the documents. The covering letter also contained the agency's contact details in case the GP or practice manager wanted to participate in the advisory board.

AstraZeneca stated that the agency contacted 80 GP practices to obtain approximately 20 attendees who met the pre-specified criteria. The final list of attendees for both advisory boards fulfilled the pre-specified criteria given to the agency which demonstrated that by this process it was able to identify eligible people and screen out when appropriate.

AstraZeneca submitted that it was difficult to know how the situation arose with the complainant as the complaint was anonymised. The agency was very clear that the process was as outlined above and it was possible that the complainant's practice received two invitations (GP and practice manager), one of which was addressed to 'Dr X' and another with no addressee, as a result of this being requested by the receptionist when telephoned by the agency. The agency was aware that the intention was to personalise the invitation with the recipient's name and did so in cases where it had spoken directly to the intended recipient. In cases where the receptionist had requested it to be sent for him/her to pass on to the relevant person, the agency admitted that due to an oversight on its part it had either not put a recipient's name on the invitation or had left it blank.

AstraZeneca accepted full responsibility for the actions and oversight of its third parties but contended that there had not been a breach of high standards in this case given the full explanation above and the validity of the advisory board. It was unfortunate that the complainant received the invitations with no context or explanation from the receptionist. AstraZeneca had described a clear rationale for the advisory boards and demonstrated that it sought to recruit a limited number of appropriate attendees using a robust recruitment strategy; the attendees were offered honoraria for their services based on the AstraZeneca fair market value for their role. AstraZeneca refuted the alleged breach of Clause 9.1.

In conclusion, AstraZeneca accepted that the complainant had experienced unintentional confusion and concern about the advisory boards but, based on the above, it refuted the alleged breaches of Clauses 9.1, 18.1 and 20.1. In addition, the company confirmed that neither the agency nor it had received a complaint from any of the other practices contacted. AstraZeneca considered that high standards were maintained when recruiting for and organising the advisory boards and that the agency followed a correct process. Also, as demonstrated, this was a legitimate advisory board, with appropriate invitees being offered honoraria that reflected their professional standing and fair market value. AstraZeneca thus refuted the alleged breach of Clause 2.

PANEL RULING

The Panel noted that it was acceptable for companies to arrange advisory board meetings and the like and to pay health professionals and others for advice on subjects relevant to their products. Nonetheless the arrangements for such meetings had to comply with the Code.

To be considered a legitimate advisory board the choice and number of participants should stand up to independent scrutiny; each should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the meeting. The number of participants at a meeting should be limited so as to allow active participation by all. The agenda should allow adequate time for discussion. The number of meetings and the number of participants at each should be driven by need and not the invitees' willingness to attend. Invitations to participate in an advisory board meeting should state the purpose of the meeting, the expected advisory role and the amount of work to be undertaken.

The Panel noted the complainant had provided copies of three invitations to an AstraZeneca advisory board, one addressed to 'Dear Dr X'; one to 'All GP's' [sic] and the other with no stated addressee; the latter invitation was, according to AstraZeneca, intended for the practice manager. The Panel noted that the invitation to 'Dear Dr X' stated that the objective of the meeting was to gain advice and feedback on new educational materials to support GPs with more effective diagnosis of bipolar disorder and how best to discuss these materials via a team of telephone-based service agents. Given the broad stated objectives the Panel noted that AstraZeneca aimed to recruit GPs from across the mental health and commissioning spectrum. The meeting objectives stated in the invitation for practice managers were similar to those above, with the additional objective of gaining advice and feedback on how the educational materials might support the practice and patients by achieving targets through increased and more accurate diagnosis. AstraZeneca had also submitted that it wanted to assess criteria upon which a practice

manager might permit access to speak to a GP directly. The Panel noted the broad objectives of the advisory board and the aim to recruit managers from a broad spectrum of practices including those with no mental health lead. According to AstraZeneca these selection criteria were met in relation to each advisory board.

The Panel noted AstraZeneca's submission that the agency initially contacted practices by telephone, but if they were not permitted to speak to a GP or practice manager then a facsimile or email was sent to the receptionist to be passed on to the relevant person. AstraZeneca submitted that in these instances the agency produced a covering letter which was sent with the invitation to ensure that it was passed to the intended recipient. The Panel noted that the two documents received by the complainant in relation to the GP advisory board were addressed to 'Dear Dr X' and 'All GP's' [sic]. The latter appeared to be a covering letter produced by the agency although the position was unclear. It did not appear to be part of the approved material for the advisory board provided by AstraZeneca. The third document, an invitation to the practice manager advisory board, did not bear an addressee. The Panel noted AstraZeneca's submission that faxes were sometimes not addressed to an individual at the request of the practice receptionist, and considered that this was unsatisfactory. The selection of participants must stand up to scrutiny. In this regard the Panel noted AstraZeneca's acknowledgement that there was an unfortunate oversight on the part of its agency in either not putting a recipient's name on the invitation or leaving it blank. The Panel noted that the identity of the complainant had not been disclosed and thus AstraZeneca was unable to comment on the arrangements in place at the complainant's practice.

The Panel noted that what appeared to be the covering letter referred only to the GP advisory board on 26 March. The practice manager invitation bore no addressee and did not make it at all clear that invitees had to be practice managers. The Panel did not know whether AstraZeneca's agency had had a telephone conversation with the complainant's receptionist about this letter and, if so, what was said. However, it would not be unreasonable for a receptionist to mistakenly assume that it was intended for any health professional or senior administrative staff employed at the practice. Indeed the complainant appeared to view the practice manager invitation as part of the information about the GP meeting.

The Panel noted the objectives of the advisory boards and consequently the broad selection criteria for participants. Given such broad selection criteria the Panel did not consider the use of the term 'All GPs' and 'Dear Dr X' in relation to a GP surgery was unreasonable, or that on the specific facts of this case the GP advisory board invitation implied that no selection had taken place as alleged. No breach of Clause 20.1 was ruled in that regard. In relation to the practice manager invitation the Panel considered that the absence of any addressee, the failure to identify the status of consultants within the letter and the absence of any relevant covering letter gave a poor impression and implied that no specific selection of consultants had or would take place. A breach of Clause 20.1 was ruled.

The Panel noted that although the educational module to be discussed at the advisory boards related to mental health, it would be made available to all GPs regardless of their expertise in that therapy area. In that regard the written brief provided to the agency engaged to recruit for the advisory boards required it to ensure that the GP advisory board was made up of 8-10 GPs, to include 1-2 clinical commissioning group mental health leads, 2-3 practice mental health leads and 4-5 GPs with no specific interest in mental health. The practice manager advisory board was to consist of those who worked in practices with GPs who had similar roles to those described above. The GP advisory board, if it had gone ahead, would have consisted of six GPs, one clinical commissioning group mental health lead, one GP that saw his own mental health patients and a mental health locality cluster lead. The practice manager advisory board, if it had gone ahead, would have consisted of five managers who worked in practices where GPs had no special interest in mental health, three who worked in practices where there was a mental health lead and two who worked in practices where there was a clinical commissioning group mental health lead. In the Panel's view, and irrespective of its ruling above about the practice manager advisory board invitation, the attendees at each advisory board had ultimately been selected such as to fairly represent the target audience for the educational materials under discussion. The Panel did not consider that an advisory board of nine or ten was a number greater than that reasonably necessary to achieve the objectives outlined above in the 3 hours available. No breach of Clause 20.1 was ruled in that regard.

The Panel noted that it was a legitimate activity for pharmaceutical companies to engage health professionals as consultants for a range of activities, including as advisory board members, and that health professionals could be paid a fee for such services. The Panel noted that both meetings had been scheduled to run from 6.30 – 9.30pm with one 15 minute break. Each agenda item outlined the discussion and feedback expected from participants. The honorarium offered in the invitation to GPs was £300 and for practice managers the honorarium offered in the invitation was £125. The Panel did not consider that these were unreasonable fees for 2 ¾ hours' work and did not consider that either payment was, in itself, an incentive to attend either meeting as alleged. No breach of Clause 20.1 was ruled.

The Panel further noted that the agency brief stated that one of the objectives of both advisory boards was to 'Gain feedback on the Seroquel offering'. The Panel assumed that this referred to the educational materials described above. The Panel considered that this was unfortunate wording to describe such materials, which should be non-promotional.

The Panel noted its comments and rulings above about the meetings' objectives and the consultants' honoraria. The Panel did not consider that the honoraria were an inducement to prescribe or recommend any medicine and consequently ruled no breach of Clause 18.1.

The Panel noted its rulings above and subsequently ruled no breach of Clauses 9.1 and 2.

Complaint received **23 March 2012**

Case completed **30 May 2012**

NORGINE v GALEN

Trustsaver campaign

Norgine alleged that Galen's Trustsaver campaign materials, namely a website, leavepiece and advertisements, contained misleading and exaggerated claims about cost savings which could be achieved by switching from certain branded market leaders (including Norgine's Movicol) to certain named Galen products.

Galen's detailed response is given below.

Norgine alleged that the cost savings calculated in an interactive 'map of savings' section of the website were misleading because, *et al*, the one year savings could only happen if 100% of patients taking the branded products were switched simultaneously to the Galen products. This would not happen. Further, the claims did not make it clear that the savings stated were only possible in year one.

The Panel noted that the Trustsaver campaign was designed to show prescribers how much they could save if they prescribed Galen's branded generic medicines instead of the more expensive branded market leaders. The campaign was simply about switching from one medicine to its less expensive generic equivalent; the only variable factor would be the acquisition cost.

The Panel noted that the homepage of the Trustsaver website stated that Galen had a range of products that offered significant savings against the market leading brands. Readers could access an interactive map of savings whereby they could find out the total potential one year savings if Galen's medicines Flotros, Laxido Orange and Calceos were prescribed instead of the current market leading brands. In the same block of text which explained how to use the interactive map, the readers were invited to click on a link which took them to a comprehensive explanation of assumptions and calculations. In all cases it was assumed that all prescriptions would be switched to the Galen products.

The Panel considered that although a 100% switch was unlikely, and those accessing the website would understand that to be so, it would, nonetheless, be seen as a goal in order to maximise any savings. The interactive map of savings clearly referred to 'Total *potential* one year savings …' (emphasis added). The Panel noted that the map of savings referred to 'one year savings' not 'year one savings'. In that regard, the Panel did not consider that an instantaneous switch was necessary; the year could start at the point when all patients had been switched. The Panel considered that in the context of demonstrating to prescribers the potential magnitude of savings that could be made in one year by prescribing Galen products, the map of savings was not misleading. The underlying assumptions were sufficiently clear. No breach of the Code was ruled.

Norgine alleged that a section of the website entitled 'Savings Calculator' exaggerated the savings that could be achieved and noted that again the calculated savings relied on an unrealistic 100% switch to Galen's product from day one.

The Panel noted that by accessing the savings calculator readers could calculate how much they would save if they switched 100% of their prescriptions from brand leaders to the equivalent Galen branded generic medicines. The Panel noted that users had to input their annual average use of the brand leader in order to calculate the average annual saving. Assumptions and calculations were clearly stated. The Panel considered that although a 100% switch was unlikely, and the target audience would understand that to be so, it would nonetheless be seen as a goal in order to maximise any savings. In that regard the Panel considered that it would be impossible to design a tool which would, with complete accuracy, predict the percentage of prescriptions that would be switched and thus calculate the potential savings. The Panel considered that within the context of demonstrating to prescribers the potential magnitude of savings that could be made in one year by prescribing a specific Galen product instead of the market leader, the savings calculator was not misleading. No breach of the Code was ruled.

Norgine noted that the leavepiece included a claim that by using three specified Galen products, an average size primary care organisation (PCO) could potentially save £270k/year. Norgine stated that as the £270k was so prominently presented, and without qualification, there appeared to be little uncertainty in the figure. To achieve this saving 100% of patients would have to be switched to Galen products overnight which would never happen. Norgine alleged that the claim was misleading and exaggerated.

The Panel noted that the leavepiece was entitled 'Master the art of saving'. Readers were informed that the Galen Trustsaver collection of six branded generics offered significant savings against current market-leading brands. The claim at issue referred to three Galen medicines (Laxido Orange, Calceos and Flotros) and stated that the average-sized PCO could potentially save £270k per year by adopting these medicines. Readers were invited to visit the Trustsaver website to calculate potential savings locally. The Panel again noted the assumption and calculations involved and the limitations thereof together with its comments above and considered that in the context of informing prescribers about

the potential magnitude of savings that could be made in one year, the leavepiece was not misleading. No breach of the Code was ruled.

Norgine noted that the advertisements included the claim 'It may look like only a few pounds saved but to the NHS it could mean £45 million' and alleged that as above, this national figure for savings was unobtainable and misleading. In reality, 100% of NHS prescribers would not switch 100% of patients to Galen medicines on day one and continue that prescribing pattern for 12 months. Norgine alleged that the claim was exaggerated.

The Panel noted that the advertisements showed two people in what appeared to be an art gallery. Three 'paintings' were Galen packshots. In the middle of the 'gallery' there was a bigger-than-life-size pile of pound coins which one of the people was studying. The headline read 'It may look like only a few pounds saved but to the NHS it could mean £45 million'. The advertisement explained that Galen products offered significant savings against the current market-leading brands. The calculations and assumptions for the claimed savings were stated and as before they relied upon a 100% switch to relevant Galen medicines. As above the Panel noted the limitation of the assumptions together with its comments above and considered that in the context of informing prescribers about the potential magnitude of savings that could be made, the advertisements would not mislead the target audience. No breach of the Code was ruled.

Norgine considered that the Trustsaver campaign was seriously flawed. It singularly failed to maintain high standards and warranted consideration of a breach of Clause 2.

The Panel noted its rulings above and consequently considered that Galen had not failed to maintain high standards. No breach of the Code was ruled. The Panel did not consider that the Trustsaver campaign was such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry. No breach of Clause 2 was ruled.

Norgine Pharmaceuticals Ltd complained about the Trustsaver campaign run by Galen Limited. Norgine alleged that the associated website, leavepiece (ref PMR-Sept-2011-0359) and advertisements in Prescriber and Nurse Prescriber (refs PMR-Feb-2012-0076 and PMR-Feb-2012-0070) contained misleading and exaggerated claims about cost savings which could be achieved by switching from certain branded market leaders (including Norgine's product Movicol) to certain named Galen products.

By way of background Norgine noted that supplementary information to Clause 7.2 stated: 'The economic evaluation of medicines is a relatively new science. Care must be taken that any claim involving the economic evaluation of a medicine is borne out by the data available and does not exaggerate its significance. To be appropriate as the basis of promotional claims, the assumptions made in an economic evaluation must be clinically appropriate …'. This was sensible guidance, as most prescribers had little or no training in health economics, and as such they might be less able to evaluate promotional cost savings claims based on economic comparisons of medicines than comparative safety or efficacy claims.

Norgine submitted that in a climate of relentless downwards pressure on NHS expenditure, it was particularly important not to mislead payers and prescribers by exaggerated claims of cost savings available by switching from one product to another. In their willingness to save money whenever and however possible, prescribers and payers were likely to be less critical of cost saving claims.

The Trustsaver campaign was based on the principle that as Galen's branded generic products were generally less expensive than the branded market leaders such as Movicol, savings could be achieved by switching to the Galen product. Norgine was, however, seriously concerned that Galen had misled prescribers as it specified very precise cash savings that could be achieved at a practice level, a primary care trust/clinical commissioning group (PCT/CCG) level and even nationally.

The Trustsaver campaign centred on the claim that medicines budgets would be reduced at all levels (practice, PCT/CCG and national) and fundamentally consisted of a budget impact analysis (BIA). Either the prescriber filled in details directly on the Trustsaver website which then calculated budget impact (savings), or aggregated savings data was produced to claim savings on a PCT/CCG level or nationally in the leavepiece and the journal advertisements respectively.

BIA was frequently used in the economic evaluation of medicines, eg to allow payers to calculate, prior to launch, what impact the introduction of a new medicine would have on their local budgets. Norgine submitted that it was important that BIA was conducted as accurately as possible to give payers and prescribers the best possible information and referred to some of the key recommendations in best practice guidelines.

Norgine submitted that calculations should look at a realistic estimate as to how the new product might penetrate the market compared with an established product. A properly conducted BIA would produce a number of scenarios for market penetration and present the budget impact of each. For example a sound model would be able to compute the budget impact in scenarios in which product A took 20%, 30%, 40%, 50%, 60%, or 70% etc of the sales of product B over a given period of time. A model that assumed 100% market penetration without scenario analyses of anything less was therefore unrealistic and invalid, as Norgine believed was the case with the Trustsaver campaign.

By way of background, Galen explained that the Trustsaver concept was introduced just over two years ago with the principle of offering a portfolio of quality medicines which could potentially benefit the

NHS in terms of cost savings, while maintaining patient care. In the time that it had been running, no health professional had complained to Galen about it. Galen noted Norgine's view that potential cost savings claims used in Trustsaver materials consisted of a BIA and that this had not been carried out properly. Galen submitted that its Trustsaver campaign was not a BIA and in that regard noted that a BIA was:

> 'an essential part of a comprehensive economic assessment of a health-care technology and is increasingly required, along with cost-effectiveness analysis (CEA), before formulary approval or reimbursement. The purpose of a BIA is to estimate the financial consequences of adoption and diffusion of a new health-care intervention within a specific health-care setting or system context given inevitable resource constraints.' (Mauskopf *et al* 2007).

Galen explained that one of the core principles of the Trustsaver campaign was that the medicines included in the portfolio were not new ones or in a new class. Each product was a quality product, containing well established active ingredients. In the potential cost savings claims the Trustsaver products were being compared 'like-for-like' with the branded market leader based on the number of equivalent packs used and the current list prices, eg Laxido Orange was the generic equivalent of Norgine's market-leading brand, Movicol but was clearly less expensive to buy than Movicol. This cost differentiation had not been challenged by Norgine. The potential cost savings claims in the Trustsaver materials were simple and straightforward cost calculations based on the purchase price of the products. The basis of the claims was made clear throughout the materials and they did not mislead the target audience.

In Galen's view, Norgine had attempted to complicate the issue by presenting the potential cost savings claims as a BIA. Laxido was not a new or unproven class of medicine and Galen had not presented these potential cost saving claims as a BIA and never referenced it as a BIA.

A Trustsaver website

1 Interactive map of savings

COMPLAINT

Norgine noted that the Trustsaver website (www.trustsaver.co.uk) contained a section entitled 'Map of Savings'. By selecting a region on the map (for example Camden) the calculator informed the user that:

> 'The potential one year saving if Flotros, Laxido Orange and Calceos are prescribed instead of other current market leading brands' will be £140,524.

Norgine alleged that for a number of reasons this claim was misleading in breach of Clause 7.2.

- The one year savings could only happen if 100% of patients taking the brand leading products were switched to the listed Galen products; this would never happen in reality. Some prescribers might be unwilling to switch some or all patients to the Galen brands and some patients might be unwilling to be switched to the Galen brands if they were happy with their current treatment.

- In order for savings of this magnitude to be achieved, 100% of patients would need to switch to Galen brands all at the same time on day one. Logistically this could never happen as some patients would need to visit their prescriber for a change to take place, and new prescriptions would need to be produced for patients on repeat prescriptions, so there would be some considerable period of phasing whilst the change to the Galen brands occurred.

- Potential savings might be achieved over the first year by switching to a less expensive medicine, but the claim did not make clear that the saving was only possible for the first year. If less expensive products were continued for subsequent years nowhere near the initial saving could be achieved.

- The saving figure was very precise (to the last £1) and therefore implied a high degree of precision in the savings calculation, when in fact this was far from the truth as BIA was not a precise science.

- No scenario analyses were presented for anything other than 100% switching.

RESPONSE

Galen submitted that the Trustsaver campaign had evolved and changed and the map of savings was not part of the current website. It was retired on 27 March 2012 due to the changing structure of the NHS.

When it existed, the map of savings used IMS data to calculate the savings available in various UK regions. The assumptions and calculations for the map of savings contained considerable and detailed information on how the savings figures were obtained for each product (Flotros, Calceos and Laxido Orange). This could be accessed via a very clear and prominent direct link.

The fact that the savings figures presented were based on a 100% conversion was made very clear in the assumptions and calculations. Indeed when the savings figure for each region was presented, the statement that accompanied it read: 'Total potential one year saving if Flotros, Laxido Orange and Calceos are prescribed instead of the other current market leading brands'.

As noted in inter-company dialogue, prescribers, budget managers and medicines management teams were all highly qualified, intelligent and experienced, and would understand that any conversion would not be instantaneous and so savings would not be realised immediately. They would also know what approximate percentage conversion they were likely to realise in their own localities. Galen had not tried to portray that a 100% conversion would definitely occur or that any conversion would happen instantaneously.

Norgine had also raised a point that these savings were only available for one year ie that if less expensive products were continued for subsequent years, nowhere near the initial saving could be achieved. However, this was not the case. The savings figures were based on what would be spent on Trustsaver products vs the market-leading brands. This held true for any subsequent years provided that prices remained constant; the assumptions made it clear that the calculations were based on NHS list prices at a certain time point. It could be argued that the savings figures vs the market-leading brands might even increase in subsequent years. Trustsaver was an evolving, changing campaign and the costs were monitored and updated when they happened, thus providing accurate potential cost savings.

It was accepted that the savings figures presented were, illustrative. However in accordance with Clause 7.2 and as good practice, Galen had tried to be as accurate as possible in an attempt to give the best indication of the potential savings available. Norgine's point about a BIA not being a precise science was not valid as this was not based on BIA as previously explained.

Similarly Norgine's complaint that no scenario analyses were presented for anything other than 100% conversion was invalid as the map of savings was not based on BIA for the reasons outlined above. Galen submitted that it had openly and transparently made it clear that the savings figures were based on a 100% conversion. Galen knew that the NHS communicated cost minimisation in varying degrees but 100% was regularly used as the initial starting point and newsletters and guidance from different NHS primary care organisations (PCOs) (an example was provided) referred to a 100% conversion target for various medicines and so basing potential savings on a 100% conversion was not unusual for illustrative purposes.

Galen denied that the Trustsaver map of savings was in breach of Clause 7.2.

PANEL RULING

The Panel noted that the Trustsaver campaign was designed to show prescribers how much they could save if they prescribed Galen's branded generic medicines instead of the more expensive branded market leaders. Galen's products were not new medicines and so in that regard the Panel did not consider that Norgine's reference to BIA was relevant. Manskopf *et al* stated that the purpose of a BIA was to estimate the financial consequences of adoption and diffusion of a new healthcare intervention within a specific healthcare setting or system context given inevitable resource constraints. The Panel noted that the Trustsaver campaign was simply about switching from one medicine to its less expensive generic equivalent – it was not about the use of a new healthcare intervention. The only variable factor would be the acquisition cost.

The Panel noted that the homepage of the Trustsaver website stated that Galen had a range of products that offered significant savings against the market leading brands. Readers could access an interactive map of savings whereby they could find out the total potential one year savings if Galen's medicines Flotros, Laxido Orange and Calceos were prescribed instead of the current market leading brands. Although the interactive map was no longer in use it had been a feature of the Trustsaver website when Norgine had submitted its complaint. In the same block of text which explained how to use the interactive map, the readers were invited to click on a link which took them to a comprehensive explanation of assumptions and calculations. In all cases it was assumed that all prescriptions would be switched to the Galen products.

The Panel considered that although a 100% switch was unlikely, and those accessing the website would understand that to be so, it would, nonetheless, be seen as a goal in order to maximise any savings. In that regard the Panel noted the NHS newsletter provided by Galen. The interactive map of savings clearly referred to 'Total *potential* one year savings …' (emphasis added). The Panel noted that the map of savings referred to 'one year savings' not 'year one savings'. In that regard, the Panel did not consider that an instantaneous switch was necessary; the year could start at the point when all patients had been switched. The Panel considered that in the context of demonstrating to prescribers the potential magnitude of savings that could be made in one year by prescribing Galen products, the map of savings was not misleading. The underlying assumptions were sufficiently clear. No breach of Clause 7.2 was ruled.

2 Laxido Orange Savings Calculator

COMPLAINT

Norgine noted that the website contained a section entitled 'Savings Calculator' which enabled users to select a specific Galen product and enter the average annual usage of a specified brand, and the website would calculate the 'average annual saving'. For example, users were invited to enter their annual average usage of Movicol 20 and 30 packs in order to calculate 'Average Annual Saving'. No guidance was given on this page about how this variable should be sourced. If users selected Laxido Orange, the screen entitled 'Laxido Orange Savings Calculator' opened. Users then entered the annual average usage of Movicol (for example 1000 units of Movicol 30) and the website calculated an 'Annual average saving' of

£1,340.00. The following assumptions and calculations were listed below the savings calculator:

'1 The NHS list price of Laxido Orange is £3.56 per 20 sachet pack and £5.34 per 30 sachet pack.

2 Equivalent Laxido Orange cost is calculated by switching the annual usage entered by brand and pack size directly to Laxido Orange at the equivalent pack size.

3 The potential savings calculated are based on the annual usage entered by brand, and assume that all units are switched to the equivalent pack of Laxido Orange.

4 All flavours of MOVICOL are priced at the prices listed above.'

Norgine submitted that the key assumption here was that all units were switched to the equivalent pack of Laxido Orange. As noted above, the scenario of 100% switch from Movicol to Laxido Orange from day one was unrealistic. Also the savings figure referred to was a maximum annual saving not an average annual saving as claimed. Norgine alleged that this section of the website exaggerated the savings which could be achieved in breach of Clause 7.2.

RESPONSE

Galen submitted that the Laxido Orange Savings Calculator was a simple tool, essentially the same as a desk calculator within the website, designed to indicate to users the cost savings that they could potentially make, based on the figures that they entered into the calculator. Users clearly must enter the 'Average annual usage' themselves, which in turn calculated the average annual saving. Users would know how to source a figure for their own 'average annual usage'.

Galen stated that one of the assumptions stated was that 'The potential savings calculated are based on the annual usage entered by brand, and assume that all units are switched to the equivalent pack of Laxido Orange'. It was clear that 'all units' referred to all of the units inputted by the user. The user could be in no doubt that the calculation was based on all units being converted. These were the possible savings based on the current list prices and reflected the fact that Laxido Orange was 20% less expensive than Movicol. This cost differentiation had not been challenged by Norgine.

Galen submitted that the fact that the user inputted the usage figures themselves was a key point. This meant that the savings calculator was very flexible as it allowed a variation in usage to be entered. Users would know what approximate degree of a conversion they were likely to realise in their own respective localities, and so could adjust their figures accordingly. As with the Map of Savings, Galen had not tried to portray that a 100% conversion would definitely occur or that any conversion would happen instantaneously. Galen submitted that data on file demonstrated that a 90%+ conversion had occurred from Movicol to Laxido Orange in practice in some areas. This could be shared with the Panel if requested. Therefore presenting potential savings figures based on a 100% conversion in an open and transparent manner was not unreasonable.

The savings figure referred to could not be a maximum annual saving as claimed by Norgine, as users only entered their 'average annual usage'. To be a maximum savings figure, users would need to input their maximum annual usage.

Galen submitted that this section of the website did not exaggerate the savings that could be achieved and so it denied a breach of Clause 7.2.

PANEL RULING

The Panel noted that by accessing the savings calculator readers could calculate how much they would save if they switched 100% of their prescriptions from brand leaders to the equivalent Galen branded generic medicines. The Panel noted that users had to input their annual average use of the brand leader in order to calculate the average annual saving. Assumptions and calculations were clearly stated. The Panel considered that although a 100% switch was unlikely, and the target audience would understand that to be so, it would nonetheless be seen as a goal in order to maximise any savings. In that regard the Panel considered that it would be impossible to design a tool which would, with complete accuracy, predict the percentage of prescriptions that would be switched and thus calculate the potential savings. The Panel considered that within the context of demonstrating to prescribers the potential magnitude of savings that could be made in one year by prescribing a specific Galen product instead of the market leader, the savings calculator was not misleading. No breach of Clause 7.2 was ruled.

B Trustsaver Collection Leavepiece

COMPLAINT

Norgine noted that the leavepiece featured the claim:

> 'With adopting Laxido Orange, Calceos and Flotros (trospium chloride) alone, an average-sized PCO (population~300,000) could potentially save per year:
>
> £270k'

Norgine noted that '£270k' was presented in much larger font size than the rest of the text of the leavepiece and was the dominant message. The assumptions and qualifications were in small font size at the foot of the piece.

In inter-company dialogue, Galen focussed on an assertion that as prescribers and budget managers were highly qualified and intelligent they would

understand that any switch would not be instantaneous and savings would not be realised immediately. But it was in the presentation of these 'savings' that the problem arose in the leavepiece. In Norgine's view, stating £270k in such a prominent manner suggested little uncertainty in the figure. The claim was bold, with no qualification and so gave the clear message that if prescribers changed to the three Galen products this was what they would save.

To achieve these savings at a PCT level 100% of patients taking other products would have to switch to the corresponding Galen product overnight and all at the same time. In practice this would never happen. Norgine alleged that the claim was misleading in breach of Clause 7.2; it exaggerated the magnitude of savings achievable.

RESPONSE

Galen submitted that the leavepiece was withdrawn some months ago as a result of feedback from the salesforce that it had not had the desired impact with customers.

Galen noted that Norgine was concerned about the prominence of the £270K savings figure presented in the leavepiece and claimed that no qualification was given and that there was a clear indication that this was what prescribers would save.

The actual claim on the leavepiece regarding this figure read: 'With adopting Laxido Orange, Calceos and Flotros (trospium chloride) alone, an average-sized PCO (population ~300,000) could potentially save per year**'. This statement appeared directly above the quoted savings figure, in bold type and in a font size larger than a lot of the other text in the leavepiece. By using a savings figure based on an average-sized PCO, especially in such a clear and transparent manner, Galen had been mindful not to exaggerate the potential savings figure.

The caveat relating to this claim which appeared on the same page, also made it clear that the figure was based on a 100% conversion and that it was the maximum potential: '**This potential saving estimate is based on IMS data for an actual PCO with a population of approximately 300,000 and reflects the maximum potential based on 100% of prescriptions available being switched over to the applicable Galen product(s). Savings based on three of the trustsaver products only and on current list prices'.

Also directly opposite the quoted savings figure was a table which contained a final column entitled 'Potential savings against current market-leading brands'. The percentage cost savings figure for each Trustsaver brand against the applicable market leader was displayed. These figures were referenced to MIMS, Chemist & Druggist, IMS Data and data on file that demonstrated how the potential savings figures were calculated.

Galen repeated that it had not tried to portray that a 100% conversion would definitely occur or that any conversion would happen instantaneously. Also prescribers would know what approximate percentage conversion they were likely to realise locally and that any conversion would happen over a period of time.

Galen noted that Norgine raised various issues with the leavepiece in the first round of inter-company dialogue. However following Galen's response, there was no reference made again to a number of these in the second letter that Galen received from Norgine. Galen believed that some of these issues had been resolved following its response.

Galen denied that the leavepiece exaggerated the magnitude of savings achievable and thus denied a breach of Clause 7.2.

PANEL RULING

The Panel noted that the leavepiece was entitled 'Master the art of saving'. The headline across the inside double page spread was 'A smart choice for saving your NHS budget'. Readers were informed that the Galen Trustsaver collection of six branded generics offered significant savings against current market-leading brands. The claim at issue referred to three Galen medicines (Laxido Orange, Calceos and Flotros) and stated that the average-sized primary care organisation could potentially save £270k per year by adopting these medicines. Readers were invited to visit the Trustsaver website to calculate potential savings locally. The Panel again noted the assumption and calculations involved and the limitations thereof together with its comments at Points A1 and A2 above and considered that in the context of informing prescribers about the potential magnitude of savings that could be made in one year, the leavepiece was not misleading. No breach of Clause 7.2 was ruled.

C Trustsaver journal advertisements

COMPLAINT

Norgine submitted that the advertisements at issue came to its attention after it had concluded inter-company dialogue with Galen, but as the concerns it had were the same as it had with the items brought up in inter-company dialogue it included it in its complaint.

Norgine noted that the advertisements contained the claim:

> 'It may look like only a few pounds saved but to the NHS it could mean £45 million.'

As with practice level savings and PCT/CCG level savings this national figure for savings was completely unobtainable and was highly misleading for the reasons stated in points A and B above. There was no way in reality that 100% of NHS prescribers would switch 100% of patients to Galen medicines on day one and continue that prescribing pattern for 12 months. Norgine considered that the claim therefore greatly exaggerated the savings that might

be made across the NHS if the Galen medicines were to be more widely used. A breach of Clause 7.2 was alleged.

Norgine stated that there were numerous reasons why an immediate 100% switch was an invalid assumption as mentioned above. Indeed some of these were reported in a PCT case study sponsored by Galen and available on the Trustsaver website. The article stated that 'The switch to Laxido from Movicol was introduced in April 2010, and by January 2011 (latest prescribing data available) 60% of prescriptions for Movicol/Laxido were prescribed as Laxido Orange', ie on the evidence presented, even with intense medicines management after 10 months there is only a 60% penetration rate for Laxido Orange. One of the reasons given for this was that there was some resistance from a small number of patients who did not like the flavour of Laxido - these patients were switched back to their preferred product by their GP. Other reasons could include time for change management, GP patient assessment and patient permission.

This PCT case study therefore showed that even with considerable work from the Medicines Management team and the local doctors, 100% switching was not possible, which undermined the fundamental assumption underlying the savings claims in the whole of the Trustsaver campaign.

Norgine submitted that it was important to appreciate that in any analysis of possible cost saving resulting from changing from one medicine to another, it was over simplistic to consider only the acquisition costs of the medicines as there might also be considerable resource and therefore additional cost implications (as was seen from the PCT case study). When conducting a cost-minimization analysis, all costs (resource expenditures) inherent to the delivery of the therapeutic intervention and that were relevant to the economic assessment should be measured. The Trustsaver campaign did not do this.

Any budget impact/cost tool must include at a minimum the core costs associated with the intervention ie costs associated with implementing change and all relevant comparators (Mauskopf *et al*). Its omission in not including fundamental basic cost components was misleading as it did not include all costs which might be involved when one product was switched to another.

A good example of the additional costs which should be considered was perfectly illustrated in the PCT case study on the Trustsaver website. The authors explained how the switch was managed:

'The introduction of Laxido Orange as an alternative drug was accompanied by written information – a detail aid – developed by the medicines management team to support all prescribers, including GPs and pharmacists.

In general:

- The medicines management pharmacist or technician identified the patients who were using Movicol.
- These patients were reviewed by their GP or practice staff, and the change to Laxido by prescribers was discussed.
- Formularies were changed on the computer system to remind patients about using Laxido Orange.
- ScriptSwitch and similar tools were used at the point of prescribing.
- When a switch was agreed, letters were sent to all patients to explain the change to their prescription.'

Therefore it was quite clear from this case study that the exercise was not instantaneous; it took some time with a considerable amount of effort required to implement this switch, all of which entailed costs (eg doctor's time, pharmacist's time, letters sent, updating IT systems).

Norgine thus considered that by just taking medicine costs into account and nothing else, and assuming 100% switch, Galen's claims greatly exaggerated the amount that might be saved in practice. Norgine alleged that the simplistic way the savings were calculated was misleading in breach of Clause 7.2.

RESPONSE

Galen submitted that the advertisements at issue had only recently been published (Date of Preparation: February 2012). Norgine had conceded that the issues that it had with these advertisements were never raised during inter-company dialogue.

Galen stated that the advertisements were part of an updated Trustsaver campaign. Although all of Galen's previous claims had complied with the Code, it reviewed these as part of the campaign update, and concluded that basing the savings claim on the current UK population was a better simplification. By using this methodology there was even less chance that a reader could misinterpret the claim. It was totally clear, open and transparent.

Galen noted that the savings figures presented in the advertisements were based on just three Trustsaver products; the potential savings figure available to the NHS based on the whole portfolio was considerably more than the £45M cited.

Galen reiterated that it was valid to base a potential savings claim on a 100% conversion. The footnote that accompanied a related claim in the advertisement read: 'This potential saving estimate was based on IMS data and reflects the maximum potential based on 100% of prescriptions available being switched over to the applicable Galen product(s). Savings based on three of the Trustsaver products only and on current list prices'. This footnote appeared in the same area of the advertisements as the potential savings claims. The

reader could be in no doubt as to what the potential savings claims were based on.

Galen denied that the advertisements exaggerated the potential savings that could be made across the NHS and it thus denied a breach of Clause 7.2.

Galen noted that Norgine had cited a PCT case study that appeared on the Trustsaver website as proof that a 100% conversion was not achievable or realistic. This case study gave a real life example of a conversion from Movicol to Laxido Orange in which the actual degree of conversion was less than the potential. Rather than proving that a 100% conversion was not possible, the inclusion of this real life case study on the website illustrated that varying degrees of conversion were possible and showed that Galen had not been misleading; the inclusion of the case study showed complete transparency.

In addition, this was only one example from one particular PCT. As previously mentioned, Galen had data on file to demonstrate that a 90%+ conversion had occurred from Movicol to Laxido Orange in practice in some areas. As previously stated this could be shared with the Panel if requested. Therefore presenting potential savings based on a 100% conversion was entirely valid.

Galen noted Norgine's submission that it was over simplistic to consider only the acquisition costs of the medicines and that when conducting a cost-minimisation analysis, all costs should be measured. However as previously explained, the potential savings claims used in the Trustsaver campaign were not part of a BIA or cost-minimisation analysis, they were part of a basic cost comparison that compared like-for-like products. An example was Laxido Orange, approved as a generic medicinal product of Movicol, yet 20% less expensive in both 20 and 30 pack sizes. As for the realisation that a conversion would not happen overnight, budget managers and medicines management teams were all highly qualified, intelligent and experienced, and would understand that resources would have to be implemented to effect a conversion. Galen also acknowledged that this would be the case. However in all of the Trustsaver materials it was made clear that the potential savings figures presented were based on medicine acquisition cost. It would be clear to health professionals that this was the case and that they would have to take account of any resources they would use in implementing a conversion. Again all calculations were accurate, open and transparent. Even after any conversion had been implemented (including any associated short-term resource costs), the savings figures were based on what would be spent on Trustsaver products vs the market-leading brands over a 12 month period.

Galen submitted that the way in which the potential savings were calculated was not misleading and so not in breach of Clause 7.2.

PANEL RULING

The Panel noted that the advertisements had not been discussed during inter-company dialogue. Nonetheless the issues raised by Norgine were so closely similar to those raised in relation to the Trustsaver website and the leavepiece, that the Panel considered that the complaint could proceed.

The advertisements showed two people in what appeared to be an art gallery. Three 'paintings' were packshots of Laxido Orange, Calceos and Flotros. In the middle of the 'gallery' there was a bigger-than-life-size pile of pound coins which one of the people was studying. The headline read 'It may look like only a few pounds saved but to the NHS it could mean £45 million'. The advertisement explained that Galen medicines offered significant savings against the current market-leading brands. The calculations and assumptions for the claimed savings were stated and as before they relied upon a 100% switch to relevant Galen medicines. As above the Panel noted the limitation of the assumptions together with its comments at Point A1 and A2 above and considered that in the context of informing prescribers about the potential magnitude of savings that could be made, the advertisements would not mislead the target audience. No breach of Clause 7.2 was ruled.

D Trustsaver campaign overall

COMPLAINT

Norgine submitted that it would be no defence of its complaints for Galen to assert that a lower standard was acceptable for health economic evaluations which were used for commercial promotion rather than for health economic evaluations used for other purposes. As noted in the Code, care must be taken that any claim involving the economic evaluation of a medicine was borne out by the data available and did not exaggerate its significance, and any assumptions made must be clinically appropriate, which clearly they were not in this case as 100% switching would never be achieved in practice.

Norgine considered the whole of Galen's BIA campaign was seriously flawed. It was out of line with guidance and good practice as to how such analyses should be conducted and presented. It singularly failed to maintain high standards in the area of economic evaluation of medicines. Therefore Norgine believed that the campaign as a whole warranted consideration of a breach of Clause 9.1.

Galen should have been aware of the misleading nature of the Trustsaver promotion, as it had the Galen sponsored PCT case study posted on the Trustsaver website. The case study showed that even with an intensive (and costly) medicines management programme, the PCT in question was only able to switch 60% of patients on Movicol to Laxido Orange over a ten month period. The continued use of claims of savings that Galen should have known was exaggerated and completely unachievable in practice, warranted consideration of a breach of Clause 2.

RESPONSE

Galen noted Norgine's submission that the significance of Galen's health economic evaluation was exaggerated and that the assumptions were not clinically appropriate as '100% switching would never be achieved in practice'. However as previously stated, the potential cost savings claims were not part of a health economic evaluation, they were part of a cost comparison. Galen had data on file to demonstrate that a 90%+ conversion had occurred from Movicol to Laxido Orange in practice in some areas. This could be shared with the Panel if requested. Galen also knew that a 100% conversion had been realised for other medicines in various areas. Galen noted Norgine's allegation that the BIA campaign was seriously flawed and out of line with guidance and good practice and failed to maintain high standards in the area of economic evaluation of medicines. Norgine had therefore alleged that the campaign was a breach of Clause 9.1.

Galen fully understood and appreciated the special nature of medicines and the professional audience to which material was directed. While Galen was not an ABPI member company (like Norgine), its systems and procedures were written to be fully Code-compliant. The company was fully committed to adhering to the Code and regularly updated materials so that potential savings claims remained up-to-date and accurate. The basis of all calculations was made very clear to the audience and the professional nature of that audience was acknowledged in that it could interpret what degree of saving it was likely to achieve in its own particular area.

The Trustsaver campaign was a high standard, quality campaign and had been well maintained and constantly updated. Galen denied a breach of Clause 9.1.

Galen noted that Norgine had concluded by alleging that Galen should have known that the Trustsaver campaign was misleading and that continued use of exaggerated savings claims which were 'completely unachievable in practice' warranted consideration of a breach of Clause 2.

Galen took the allegation of a breach of Clause 2 particularly seriously as was demanded by the nature of the clause. Norgine had again referred to the PCT case study as a basis for citing a breach of this clause. As previously stated, this case study gave a real life example of a conversion from Laxido Orange to Movicol in which the actual degree of conversion was less than the potential. The inclusion of this real life case study on the Trustsaver website illustrated that Galen had not been misleading. In commissioning this article, Galen accepted that any degree of conversion could potentially be presented along with the fact that the article might include negative as well as positive feedback on Galen Trustsaver medicines. This was demonstrated by the inclusion of reasons why there was some resistance to a conversion from Movicol to Laxido Orange, such as patients not liking the flavour of Laxido. Therefore the article was entirely balanced and did not exaggerate the degree of a conversion that was possible in practice.

However, as previously explained, this was only one example from one particular PCT and data on file demonstrated that a 90%+ conversion had occurred from Movicol to Laxido Orange in practice in some areas. Therefore presenting potential savings based on a 100% conversion was entirely valid. Galen had data on file to demonstrate that a much higher degree of conversion actually had been achieved in practice and that a 100% conversion was indeed possible. This data could be shared with the Panel if requested.

Galen submitted that rather than bring discredit upon, and reduce confidence in, the industry, the Trustsaver campaign had demonstrated how a pharmaceutical company could work with the NHS in order to bring about a cost benefit to the health service whilst maintaining patient care. A measure of how well the campaign had been accepted by health professionals was demonstrated by the degree of adoption across the UK of products from the Trustsaver portfolio, and the fact that Galen had not received a single complaint from a health professional in the two years that the campaign had run.

Therefore Galen totally refuted the alleged breach of Clause 2 and considered that this was a malicious attempt by Norgine to discredit an effective and compliant campaign.

PANEL RULING

The Panel noted its rulings above and consequently considered that Galen had not failed to maintain high standards. No breach of Clause 9.1 was ruled.

The Panel did not consider that the Trustsaver campaign was such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry. No breach of Clause 2 was ruled.

Complaint received **23 March 2012**

Case completed **29 June 2012**

PHARMACIST v ALK-ABELLÓ

Alleged conduct of a representative

A pharmacist complained about information given to him by a named ALK-Abelló representative about Jext and EpiPen, both of which were adrenaline auto injectors. Jext was marketed by ALK-Abelló and EpiPen was marketed by Meda Pharmaceuticals. Both products were indicated for the emergency treatment of anaphylaxis. According to the respective summaries of product characteristics (SPCs), Jext was activated by a 'place and push' technique and EpiPen by a 'swing and jab' motion.

The complainant alleged that the ALK-Abelló representative had told him that EpiPen, which had previously been on the formulary, had been discontinued, which was not so. Further that the route of administration of Jext was identical to that of EpiPen. The complainant reviewed the SPC for Jext and considered this claim was incorrect and could be the difference between life and death. Finally, the complainant was told that Jext had a 24 month shelf life once it reached the pharmacy, but this was incorrect; some Jext on his shelf only had a shelf life of 14 months.

The detailed response from ALK-Abelló is given below.

The Panel noted that the parties' accounts differed. The complainant stated that he and the ALK-Abelló representative met at his pharmacy on a specified date in mid-January. ALK-Abelló submitted very detailed evidence that neither the named representative nor any other representative had called on a pharmacist with the same initial and surname as the complainant on that date. Although the named representative had been at an evening meeting on that day, the complainant had stated that he was not at that meeting. The Panel had to make a ruling on the evidence before it. The complainant had the burden of proving his complaint on the balance of probabilities. ALK-Abelló's comprehensive review suggested that the complainant and the named representative had not met. The Panel considered that, on the balance of probabilities, the complainant had not proven there had been a meeting between him and the representative and thus the allegations that the representative had misled the complainant were ruled not to be in breach of the Code.

A pharmacist complained about information given to him about Jext and EpiPen, both of which were adrenaline auto injectors. Jext was marketed by ALK-Abelló Limited and EpiPen was marketed by Meda Pharmaceuticals. Both products were indicated for the emergency treatment of anaphylaxis. According to the respective summaries of product characteristics (SPCs), Jext was activated by a 'place and push' technique and EpiPen by a 'swing and jab' motion.

COMPLAINT

The complainant alleged that he had been told by an ALK-Abelló representative that EpiPen, which had previously been on the formulary, had been discontinued. On further investigation the complainant discovered that this was incorrect and the medicine was still available. The complainant further alleged that he was told not to worry about the route of administration of Jext as it was identical to that of EpiPen. The complainant reviewed the Jext SPC and considered this claim was incorrect and could be the difference between life and death. Finally, the complainant alleged that he was told that Jext had a 24 month shelf life once it reached the pharmacy, but he considered that this was incorrect; the complainant noted that he had Jext on his shelf with a 14 month shelf life.

The complainant had spoken to local colleagues and those in neighbouring primary care trusts (PCTs) and was concerned that this information could lead to a fatality. The complainant stated that his patients were extremely concerned and would rather have a medicine with which they were familiar.

The complainant could only provide the first name of the representative in question; he stated which county he worked in but not the address of his pharmacy.

When writing to ALK-Abelló, the Authority asked it to respond in relation to Clauses 2, 7.2, 7.3, 15.2 and 15.9 of the Code.

RESPONSE

ALK-Abelló stated that the only contact between an ALK-Abelló representative and any pharmacist with the same initial and surname as the complainant was at a meeting in late January 2012 organised by the Local Pharmaceutical Committee (LPC) to update local pharmacists on the support available to health professionals and patients following the PCT's decision to recommend Jext as the adrenaline auto injector of choice. There had never been any one-to-one dialogue or other contact between any ALK-Abelló representative and anyone with the same initial and surname as the complainant in the locality outside of this meeting.

ALK-Abelló submitted that in December 2011 the local PCT recommended that Jext was prescribed as the preferred adrenaline auto injector from February 2012. A detailed letter was sent from the PCT in December 2012 to all community pharmacy contractors to outline the process for this change (copy provided). That letter advised that stocks of EpiPen be reduced. Nowhere was it stated or implied that EpiPen had been discontinued. In

January 2012 the same letter was sent to all community pharmacists with a letter from ALK-Abelló, a pad of patient information leaflets, a Jext simulator and a Jext training DVD (copies were provided).

ALK-Abelló stated that the LPC hosted two identical evening training meetings in January 2012 which were attended by approximately 60 pharmacists. A delegate with the same initial and surname as the complainant attended the second meeting. The ALK-Abelló representative named by the complainant gave a brief presentation on anaphylaxis and Jext which included a video demonstration of the correct use of Jext (a copy was provided). The audience then practised the correct activation of Jext using simulators provided.

ALK-Abelló submitted that no ALK-Abelló representative had ever made any of the statements alleged by the complainant.

With regard to the injection method, ALK-Abelló submitted that the LPC had taken the switching of the preferred adrenaline auto injector to Jext as an opportunity to improve community pharmacists' knowledge of anaphylaxis and the use of adrenaline auto injectors. Pharmacists were ideally placed to ensure patients were able to correctly use an adrenaline auto injector as it was well documented that training of patients and health professionals needed to improve. The entire meeting, together with all of the supporting materials provided, demonstrated and reinforced the correct use of Jext.

ALK-Abelló noted that, whilst Jext was always promoted for use as per its SPC [place and push], it would activate correctly if used as per the EpiPen SPC [swing and jab].

In relation to shelf life, ALK-Abelló stated that the letter from the LPC, all of the materials provided by ALK-Abelló and the presentation given by the ALK-Abelló representative in question described shelf-life from date of manufacture.

ALK-Abelló submitted that the above had been confirmed by a representative of the LPC present at both of the January meetings (a copy of an email was provided).

ALK-Abelló therefore refuted the alleged breaches of Clauses 2, 7.2, 7.3, 15.2 and 15.9 of the Code.

FURTHER INFORMATION FROM THE COMPLAINANT

Following a request for further information on his recollection of the representative's comments in relation to the administration of Jext compared with EpiPen, the complainant stated that 'The event occurred at my pharmacy and not at the event. In fact it was before the event'. The complainant confirmed that he met the representative in question in mid-January and that he did not attend the LPC meeting in late January as he was out of the country.

FURTHER INFORMATION FROM ALK-ABELLÓ

Following a request for further information, ALK-Abelló submitted that the representative in question always specifically trained 'place and push', and discussed 'swing and jab' only when raised by the customer. Following a further request for more information, ALK-Abelló submitted that it only had one ALK-Abelló employee with the same first name as that provided by the complainant. The representative's local PCT had decided to switch from EpiPen to Jext as the adrenaline auto injector of choice and so the representative's name appeared on Jext information received by health professionals in the region. The representative had not visited any retail pharmacy in the area; the representative's only contact with retail pharmacists had been at two identical LPC meetings in January. The attendee list for the first meeting indicated that no one with the complainant's name had attended (copy provided).

ALK-Abelló submitted that in mid-January, on the date the complainant claimed to have met the named representative at his pharmacy, the representative had first had an afternoon meeting with a nurse specialist group and then the LPC evening meeting described above (approval forms and delegate lists were provided). The rest of the representative's day was spent travelling.

ALK-Abelló submitted information to indicate that none of its representatives visiting pharmacies in the region could have been confused with the representative in question (they either had a very different first name or were a different gender).

Records of every UK pharmacist with the same initial and surname as the complainant ever visited at their pharmacy by an ALK-Abelló representative were provided. None of those visits were on the date the complainant claimed to have met the representative in question.

Copies of the relevant training materials were provided.

PANEL RULING

The Panel noted that the parties' accounts differed. The complainant stated that he and a named ALK-Abelló representative met at his pharmacy in mid-January. ALK-Abelló had submitted very detailed evidence that neither the named representative nor any other of its representatives had called on a pharmacist with the same initial and surname as the complainant on that date. The complainant's name was not on the delegate list for the first evening meeting in January. Someone with the same initial and surname as the complainant had attended the second evening meeting organised by the named representative in late January but the complainant had stated that it was not him as he was out of the country. Despite repeated requests the complainant had not provided details of his address. ALK-Abelló submitted that the pharmacists in the relevant region

visited on the date in question were called upon by representatives of a different gender to the representative in question. The Panel had to make a ruling on the evidence before it. The complainant had the burden of proving his complaint on the balance of probabilities. ALK-Abelló's comprehensive review suggested that the complainant and the named representative had not met. The Panel considered that, on the balance of probabilities, the complainant had not proven there had been a meeting between him and the named representative and thus the allegations that the representative had misled the complainant were ruled not to be in breach of Clauses 7.2, 7.3, 15.2, 15.9 and 2.

Complaint received **26 March 2012**

Case completed **6 June 2012**

PHARMACOSMOS v VIFOR

Competitor dosing information

Pharmacosmos explained that it and Vifor differed in their interpretation of the dosing information given in the Monofer (iron isomaltoside, marketed by Pharmacosmos) summary of product characteristics (SPC). Monofer was for the parenteral treatment of iron deficiency anaemia; Vifor marketed a competitor product. Pharmacosmos alleged that Vifor representatives had told health professionals that a total dose infusion of Monofer was subject to a maximum total dose of 1,000mg which was not so. Pharmacosmos was concerned that training and briefing material encouraged the Vifor representatives to breach the Code in that regard.

The detailed response from Vifor is given below.

The Panel noted that, in support of its allegation, Pharmacosmos had reproduced part of an anonymised undated email from a health professional. It did not provide the original email. No other evidence was provided. The Panel noted that the complainant had to establish its case on the balance of probabilities.

The Panel noted that according to its SPC, Monofer could be administered as a total dose infusion given as a single dose of up to 20mg iron/kg body weight as an intravenous drip infusion. If the total iron dose exceeded 20mg iron/kg body weight, the dose must be split into two administrations with an interval of at least one week. No upper dose limit was explicitly stated.

The Panel noted Vifor's submission that it had not instructed its staff to discuss a maximum dose of Monofer. All materials that referred to Monofer dosing were withdrawn between October and December 2011. According to Vifor, discussions by its representatives on Monofer dosing were restricted to the Monofer SPC; in April 2012 representatives were advised by email to refer queries about Monofer dosing to Pharmacosmos or to the Monofer SPC. They were told that they must not offer any interpretation of the Monofer SPC or advice on dosing or administration of any competitor product. A slide for the May sales conference gave similar guidance. The Panel was concerned that given Vifor had stated its position during inter-company dialogue in December 2011, the earliest written guidance to its representatives was in April 2011, some 2 days before Pharmacosmos' complaint was received by the Authority. However, taking into account its concerns and comments above the Panel did not consider that Pharmacosmos had established that Vifor representatives had, on the balance of probabilities, commented on Monofer dosing as alleged or had been briefed to do so. No breach of the Code was ruled.

Pharmacosmos A/S complained about information given by Vifor Pharma UK Limited about the dosing of Pharmacosmos' product, Monofer (iron isomaltoside). Monofer was indicated for the treatment of iron deficiency anaemia when oral iron preparations were ineffective or could not be used or where there was a clinical need to deliver iron rapidly. Vifor marketed Ferinject (iron as ferric carboxymaltose) for the treatment of iron deficiency when oral preparations were ineffective or could not be used.

Inter-company dialogue had been unsuccessful.

COMPLAINT

Pharmacosmos stated that it and Vifor had different interpretations in respect of the dose of Monofer.

Pharmacosmos explained that Monofer could be administered as an intravenous bolus injection, a total dose infusion in which the total iron dose was given in a single administration or an intravenous infusion of a fixed 200-1000mg dose weekly until the total iron dose had been administered. The calculation of the correct dose was important for patient safety and the summary of product characteristics (SPC) identified a specific calculation. The dose required might determine the manner of administration:

Bolus injection
A 100mg-200mg slow injection given over a minimum of 2-4 minutes (up to 50mg/min), repeated up to three times a week.

Intravenous infusion of a 200-1,000mg fixed dose
This involved the product being given via an infusion (drip). The infusion time depended on the dose being administered and body weight. The dose per infusion was 200mg-1,000mg, repeated once a week until the total iron dose had been administered.

Total dose infusion (hospital only)
The entire required iron dose was given in one infusion up to 20mg/kg. If the required dose exceeded 20mg/kg the dose must be split in two infusions given at least one week apart. The infusion time depended on the dose being administered and body weight.

Pharmacosmos submitted that the description of Monofer dosing was also part of the Scottish Medicines Consortium evaluation of Monofer which was provided.

Pharmacosmos stated that at the heart of the matter was the dose that could be administered by total dose infusion. Vifor had alleged that this technique

was subject to a maximum total dose of 1,000mg. Pharmacosmos had assured Vifor that this was not so and that its reading of the SPC was incorrect. Despite this, Pharmacosmos submitted that it had anecdotal evidence that Vifor representatives continued to advise health professionals that total dose infusion was subject to a maximum dose of 1,000mg.

One email from a health professional stated:

> 'Vifor are saying that the SPC states that you can only give 1,000mg as a drip infusion which is the same thing as a total dose and the total dose states that the most you can is 20mg/per kg I just need this to be cleared up. What is the right answer a max of 1,000mg or is it 20mg/per kg'.

Pharmacosmos stated that it was not appropriate for competitors to communicate incorrect dosing information to health professionals in obvious and deliberate contradiction to what the manufacturers of that product had clearly stated was the correct interpretation of the licence.

Pharmacosmos requested in writing in November and 6 December 2011 clarification that Vifor's information to health professionals or its representative training did not include information about a dosing maximum of 1,000mg for Monofer when administered in a hospital setting.

Vifor acknowledged in December, that representatives would restrict discussions to the Monofer SPC. However, Pharmacosmos contended that this was an attempt to deflect its legitimate concerns – as Vifor had previously stated that its interpretation differed from that of Pharmacosmos, therefore Vifor had effectively stated that it would not change its position. As Vifor's interpretation of the licence differed from that of Pharmacosmos, Pharmacosmos considered that the information given to and by the Vifor representatives was incorrect and thus misleading.

In February, Pharmacosmos sought specific confirmation of the information given to Vifor employees in relation to the dose: 'Please clearly confirm that Vifor UK acknowledges the possibility to give Monofer in doses up to 20mg/kg without an absolute dose limit of 1,000mg or any other absolute dose limit. Please also confirm that you have instructed your sales force and other relevant staff accordingly'.

In its response in March Vifor repeated that it would restrict discussions to the Monofer SPC. The company did not respond specifically to the question raised about an absolute dose limit of 1,000mg. Pharmacosmos therefore considered that inter-company dialogue had not resolved this matter.

Specifically Pharmacosmos was concerned that training and briefing material provided by representatives had encouraged them to breach the Code, in breach of Clause 15.9. While Pharmacosmos did not have copies of the training material, the inter-company responses were such that it believed that Vifor had either communicated the incorrect dosing of Monofer to its representatives, or had failed to communicate the correct dose following written clarification from Pharmacosmos. To fail to provide the correct information would result in incorrect and therefore misleading information about a competitor product (Monofer).

Pharmacosmos stated that it was clearly concerned about the communication by [Vifor] representatives to health professionals. Pharmacosmos was reluctant to approach customers to ask them to get involved in an inter-company dispute. Hence it had restricted its comments on this occasion to the briefing material (or the failure to issue briefing material) by Vifor and the anonymised quotation from a physician's email to its UK medical information service.

While it understood that its interpretation of the licence differed from Vifor's, Pharmacosmos could not allow Vifor to provide prescribers with incorrect information about Pharmacosmos products. As the licence holder, Pharmacosmos was responsible for ensuring that health professionals appreciated the correct dose of its products. When other companies communicated a different position this caused confusion and therefore risked patient safety and good medical practice.

RESPONSE

Vifor submitted that it took all matters related to the Code very seriously. It recognised that it and Pharmacosmos had a difference of opinion regarding the Monofer dosing wording contained within the current SPC and as such Vifor had requested clarity from Pharmacosmos. The information provided by Pharmacosmos did not clarify the position. Discussions about gaining clarity were contained within inter-company dialogue and thus did not transfer to any briefings to representatives or within material.

In the absence of clarification from Pharmacosmos, Vifor had not briefed or trained staff to discuss a maximum dose of Monofer. To avoid confusing health professionals Vifor restricted any discussions on Monofer dosing to the product's SPC as stated in letters sent to Pharmacosmos in December 2011 and March 2012 and thus considered that inter-company dialogue had been successful.

Vifor recognised that the briefing of staff could have occurred in January 2012, however all promotional material that referred to Monofer dosing was withdrawn from use during October and December 2011. Vifor stated that current materials did not refer to Monofer dosing and staff were instructed to directly refer any questions about Monofer dosing to the product SPC or to the Pharmacosmos medical information department.

Vifor submitted that the sales force had been briefed by email in April 2012 and instruction had been

incorporated into the company initial training course. The same direction was further emphasised at the sales conference in May 2012; the relevant slide was provided.

Pharmacosmos referred to an email from a health professional requesting clarity on the dosing regimen for Monofer after a statement that Vifor had referred to the product SPC. Vifor could not verify or investigate this as no details of date or location were provided or any indication that this was given verbally or in writing to the health professional. Vifor therefore submitted that the use of such anecdotal reference was inappropriate particularly when followed with the allegation that Vifor had communicated incorrect dosing information to customers when this was neither substantiated nor verified. All staff had been instructed to refer any query regarding dosing to the Monofer SPC or Pharmacosmos medical information.

Vifor submitted that Pharmacosmos had highlighted specific concerns regarding training and briefing materials to representatives which was alleged to encourage breaches of the Code; Clause 15.9 was referred to. Vifor noted that Pharmacosmos did not have specific copies of the training material and as such had produced no evidence to support the allegation. Vifor repeated that no representative training material or briefing documents had been produced or supplied that communicated incorrect dose information for Monofer and as such Vifor had not and did not encourage staff to breach the Code in letter or spirit.

PANEL RULING

The Panel noted Vifor's submission that inter-company dialogue had been successful. The Panel noted Vifor's submission in inter-company dialogue that it would restrict any discussions on Monofer to its SPC. Vifor however, despite being asked to do so, did not clarify what its interpretation of the Monofer SPC was with regard to the subject of the complaint, ie the maximum total dose that could be administered via the total dose infusion method. This was not helpful and in this regard inter-company dialogue had been unsuccessful. The case preparation manager had referred the complaint to the Panel for consideration.

The Panel noted that Pharmacosmos had alleged that Vifor representatives had advised health professionals that the Monofer total dose infusion was subject to a maximum dose of 1000mg and that it had anecdotal evidence in this regard. In support it reproduced part of an anonymised undated email from a customer. It did not provide the original email. No other evidence in relation to activities in the UK was provided. The Panel noted that the complainant had to establish its case on the balance of probabilities.

The Panel noted that according to its SPC, Section 4.2 Posology and method of administration, Monofer could be administered as a total dose infusion given as a single dose of up to 20mg iron/kg body weight as an intravenous drip infusion. If the total iron dose exceeded 20mg iron/kg body weight, the dose must be split into two administrations with an interval of at least one week. The Panel noted that in relation to the intravenous drip infusion Monofer could be administered in doses of 200-1000mg once a week. The Panel noted that no upper dose limit was explicitly stated in the subsection which discussed total dose infusion.

The Panel noted Vifor's submission that it had not briefed or trained staff to discuss a maximum dose of Monofer. All materials that referred to Monofer dosing were withdrawn between October and December 2011. According to Vifor, discussions by its representatives on Monofer dosing were restricted to the Monofer SPC and it referred to its comments in this regard in inter-company dialogue in December 2011 and March 2012. The Panel noted that representatives were advised by an email dated 11 April 2012, and flagged as high importance, to refer queries about Monofer dosing to Pharmacosmos or to the Monofer SPC. They were told that they must not offer any interpretation of the Monofer SPC or advice on dosing or administration of any competitor product. A slide for the May sales conference made a similar comment and advised representatives not to provide any opinion or advice on Monofer dosing. The Panel was concerned that given Vifor had stated its position during inter-company dialogue in December 2011, the earliest written guidance to its representatives was in April 2011, some 2 days before Pharmacosmos' complaint was received by the Authority. However, taking into account its concerns and comments above the Panel did not consider that Pharmacosmos had established, on the balance of probabilities, that Vifor representatives had commented on Monofer dosing as alleged or had been briefed accordingly. No breach of Clause 15.9 was ruled.

Complaint received **13 April 2012**

Case completed **28 June 2012**

CASE AUTH/2498/4/12

SANDOZ v MERCK SERONO

Patient support item

Sandoz alleged that a rucksack with a removable cool bag, given as a patient support item by Merck Serono in association with Saizen (somatropin – a growth hormone used, *et al*, in children) was not related to the treatment of growth hormone deficiency and did not otherwise directly benefit patient care. Sandoz noted that Merck Serono had successfully complained about a rucksack it had provided (Case AUTH/2451/11/11) but then continued to use a similar item itself.

Merck Serono's detailed response is below.

The Panel noted that the rucksack was supplied with a self-contained cool bag which was attached to the outside of the rucksack. The Panel disagreed with Merck Serono's submission that the rucksack and cool bag constituted a single item; the cool bag had its own carrying handle and could be used independently.

The Panel noted Merck Serono's submission that the rucksack was required to contain additional equipment such as needles and a sharps bin; the company had placed a 0.45 litre sharps bin in the sample rucksack provided to the Authority. Although in the Panel's view the sharps bin provided was larger than required for weekend/holiday use, there was still plenty of room left in the rucksack for a child to pack almost all he/she would need for an overnight stay. The rucksack had a capacity of at least 10 litres. The cool bag had a capacity of approximately 2.5 litres and so the Panel queried whether it could have been designed to hold a small sharps bin, needles and the Saizen administration device.

The Panel considered that the rucksack and cool bag were two separate items. Reconstituted Saizen had to be stored at 2° - 8°C. The rucksack would not be appropriate for storing Saizen and was very much larger than needed to carry needles and a small sharps bin. The Panel did not consider that the rucksack was related to the treatment of growth hormone deficiency or otherwise benefited patient care. A breach of the Code was ruled.

During the consideration of this case the Panel was very concerned to note that although Merck Serono had successfully complained about the provision of rucksacks as patient support items by Sandoz, it had continued to provide rucksacks of its own despite inter-company dialogue. The Panel considered that such conduct demonstrated a cynical disregard for upholding the Code and the principles of self regulation, and requested that Merck Serono be advised of its concerns in this regard.

Sandoz Ltd complained about a Saizen (somatropin) patient support item provided by Merck Serono Limited. Saizen was indicated for, *et al*, growth failure or disturbance in children and adolescents. The item at issue was a rucksack with a removable cool bag.

COMPLAINT

Sandoz referred to Case AUTH/2451/11/11 in which Merck Serono complained about the rucksacks which Sandoz had provided to patients being treated with its product Omnitrope (somatropin). Sandoz was ruled in breach of the Code. Since then Sandoz had been in inter-company dialogue with Merck Serono regarding the withdrawal of Merck Serono's rucksacks. Sandoz believed the continued use of the rucksacks breached Clause 18.2. Merck Serono successfully complained about a patient support item provided by Sandoz and had then continued to use a similar item itself. Sandoz alleged that such behaviour showed a cynical disregard for the Code and brought discredit to the industry. Merck Serono had claimed that as its rucksack had a built-in cool bag it did not breach Clause 18.2.

Sandoz noted that the cool bag could be detached from the rucksack leaving two separate items, a cool bag and a rucksack. Until the ruling in Case AUTH/2451/11/11, Sandoz also provided a cool bag and a rucksack, the only difference between the Merck Serono and Sandoz systems was that the cool bag supplied by Sandoz did not attach to the outside of the rucksack by Velcro but went inside the rucksack.

Sandoz submitted that material provided by Merck Serono demonstrated that both the medicine and device were carried in the cool bag and not the rucksack. As was applicable to the Sandoz system, the rucksack provided by Merck Serono was not appropriate for storing the medicine and a cool bag was provided for this purpose. Consequently there was no requirement for a separate rucksack.

Sandoz thus failed to understand how the rucksacks provided by Merck Serono did not also breach Clause 18.2 as they were not related to the treatment of growth hormone deficiency and did not otherwise directly benefit patient care.

RESPONSE

Merck Serono submitted that in Case AUTH/2451/11/11 one of the decisions the Panel made was whether the provision of the items in question from Sandoz individually met the requirements of the Code with regard to patient support items. Merck Serono submitted that its rucksack, which had an integral cool bag compartment, constituted a single individual item, was part of a patient support programme, was supplied for a clear and specific

purpose related to the disease, was inexpensive and directly benefited patient care, and as such did not breach Clause 18.2.

Merck Serono stated that Saizen had to be carried in a temperature controlled environment with one of three devices for administration, cool.click, easypod or one.click, together with ancillary equipment such as needles and a sharps bin.

Merck Serono submitted that the rucksack ensured that Saizen was maintained at a temperature of between 2° - 8°C when travelling for up to four hours in the cool bag section which was securely attached through two clips. The cool bag could be detached for ease of packing but both parts were designed to be used together with the body of the rucksack containing the additional equipment. A sharps bin was included in the rucksack provided as an example of how this section would be used.

Adherence was critical for successful treatment with growth hormone. The rucksack was to be used when a child slept away from home, either at weekends or on holiday, to maximise adherence and as such was directly related to the treatment of growth hormone deficiency. The rucksack was part of a wider patient support programme which included patient support nurses, a telephone helpline and an online resource providing support through a website.

Merck Serono submitted that the rucksack was an individual item which helped maximise adherence with growth hormone treatment, was part of a formal patient support programme and therefore complied with Clause 18.2.

PANEL RULING

The Panel noted that Clause 18.2 stated that health professionals might be provided with items which were to be passed on to patients and which were part of a formal patient support programme, the details of which had been appropriately documented and certified in advance as required by Clause 14.3. The items provided must be inexpensive and directly benefit patient care. The supplementary information to Clause 18.2, Items Given to Patients, noted that the items should be, *et al*, related to either the condition under treatment or general health.

The Panel noted that the rucksack was supplied with a self-contained cool bag which was attached to the outside of the rucksack by two clips and strips of Velcro. The Panel disagreed with Merck Serono's submission that the rucksack and cool bag constituted a single item supplied for a clear and specific purpose related to the disease. The cool bag had its own carrying handle and could be used independently.

The Panel noted Merck Serono's submission that the rucksack was required to contain additional equipment such as needles and a sharps bin; the company had placed a 0.45 litre sharps bin in the sample rucksack provided to the Authority. Although in the Panel's view the sharps bin provided was larger than required for weekend/holiday use, there was still, nonetheless, plenty of room left in the rucksack for a child to pack almost all he/she would need for an overnight stay away from home. The rucksack had a capacity of at least 10 litres. In the Panel's view this was not commensurate with the size of the sharps bin required. The cool bag had a capacity of approximately 2.5 litres and in that regard the Panel queried whether it alone could not have been designed to hold a small sharps bin, needles and the Saizen administration device.

The Panel considered that the rucksack and cool bag were two separate items. Reconstituted Saizen had to be stored at 2° - 8°C. The rucksack would not be appropriate for storing Saizen and was very much larger than needed to carry needles and a small sharps bin. The Panel did not consider that the rucksack was related to the treatment of growth hormone deficiency or otherwise benefited patient care. A breach of Clause 18.2 was ruled.

During the consideration of this case the Panel was very concerned to note that although Merck Serono had successfully complained about the provision of rucksacks as patient support items by Sandoz (Case AUTH/2451/11/11), it had continued to provide rucksacks of its own despite inter-company dialogue. The Panel considered that such conduct demonstrated a cynical disregard for upholding the Code and the principles of self regulation, and requested that Merck Serono be advised of its concerns in this regard.

Complaint received **16 April 2012**

Case completed **23 May 2012**

CASE AUTH/2499/4/12

PHARMACIST ADVISER v SANOFI

Mozobil email

A pharmacist adviser for a specialised commissioning group complained about an email sent by a haematology sales representative from Sanofi to a hospital clinician in relation to the local funding arrangements for Genzyme's medicine Mozobil (plerixafor). Mozobil was indicated to enhance the mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in certain patients with lymphoma and multiple myeloma. Genzyme was a Sanofi company.

The email advised the clinician to submit an individual funding request (IFR) for Mozobil to the primary care trust (PCT) and 'they will approve it'. Furthermore, the representative suggested that this should be the approach 'at the minute' until 'the [specialised commissioning group] give clarity' about the source of funding. The complainant stated that the email was inappropriate, unhelpful and inaccurate.

The detailed response from Sanofi is given below.

The Panel noted the complainant's submission that a communication from his commissioner colleague had highlighted the regional policy agreed with local commissioners and described the differences in funding sources due to existing contractual arrangements. The Panel further noted Sanofi's submission that there was evidence that the clarity around contractual arrangements referred to by the complainant did not exist.

Sanofi provided a number of emails between the representative and clinicians all of which appeared to be about whether regional funding for Mozobil had been agreed.

The Panel considered that the emails received by the representative in response to her enquiries indicated that whilst there was some confusion about funding it was possible for clinicians to apply to the relevant PCT for funding for Mozobil.

The Panel considered that, contrary to the complainant's assertion, it was not necessarily inappropriate for the representative to discuss funding issues with health professionals so long as such discussions complied with the Code. However, the Panel was concerned that the representative had stated in the email at issue that the PCT 'will approve' the IFR. This was a broad claim and inappropriate as alleged. The email responses submitted by Sanofi from clinicians based in the area indicated that there was no certainty as to whether an IFR would be successful. The representative's email was therefore misleading in that regard and a breach was ruled. It was not the representative's role to reassure health professionals that every request would be funded, nor could the representative be certain that every request would be funded. The Panel considered that the representative had not maintained a high standard of ethical conduct and a breach of the Code was ruled.

A pharmacist adviser for a specialised commissioning group, complained about the conduct of a haematology sales representative from Sanofi. The matter involved funding arrangements for Genzyme's medicine Mozobil (plerixafor). Mozobil was indicated to enhance the mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in certain patients with lymphoma and multiple myeloma.

COMPLAINT

The complainant provided a copy of an email sent by the representative and alleged that the representative's intervention in local discussions about funding arrangements for Mozobil was inappropriate. The complainant was concerned that correspondence which he had been copied into, sent by the representative to a member of staff at a hospital trust, gave incorrect advice and highlighted ignorance of local NHS contracting arrangements.

Following a number of emails to the commissioning group of which the complainant was a member, from clinicians about the funding of Mozobil in one part of the region, one of the complainant's colleagues emailed relevant stakeholders in November 2011 to clarify current contractual arrangements for stem cell transplant services and, in particular, the funding of Mozobil. This highlighted the regional commissioning policy for the medicine agreed with local commissioners in July 2011 and described the differences in funding sources due to existing contractual arrangements. Having a commissioning policy agreed aimed to avoid clinicians making individual funding requests (IFRs) to patients' primary care trusts (PCTs). Yet, in March 2012, the representative advised one clinician by email to submit an IFR to the PCT and 'they will approve it'. Furthermore, the representative suggested that this should be the approach 'at the minute' until 'the [specialised commissioning group] give clarity' about the source of funding.

The complainant stated that this intervention was unhelpful and inaccurate. Rather than contribute to the ignorance in this situation, the representative should have realised the limitation of her knowledge and referred the clinician to a more appropriate NHS contact.

Genzyme was a Sanofi company. When writing to Sanofi, the Authority asked it to respond in relation to Clauses 7.2 and 15.2 of the Code.

RESPONSE

Sanofi explained that a general policy for the use of Mozobil across the strategic health authority in question was established in July 2011 by the relevant specialist commissioning group (a copy of the document was provided). Sanofi submitted that this document did not make the financial arrangements for Mozobil clear and so there had been continued confusion about the provision of Mozobil in the local hospitals trust for patients undergoing bone marrow transplant.

Sanofi submitted that there was evidence that the clarity around contractual arrangements mentioned by the complainant did not exist. Clinicians based at the region had stated that this confusion had prevented timely treatment of a patient group who would benefit from Mozobil.

Genzyme, and more recently Sanofi, had tried to engage with the regional cancer network to clarify the situation and develop a solution to an obvious blockage which prevented clinicians accessing Mozobil for their patients.

Sanofi submitted that the representative in question sent the emails in good faith; they reflected her understanding of the funding position.

Sanofi denied any breach of Clauses 7.2 or 15.2.

PANEL RULING

The Panel noted that according to the complainant an email had been sent in November 2011 by his commissioner colleague to relevant stakeholders to clarify contractual arrangements for stem cell transplant services and in particular the funding of Mozobil. The complainant had stated that the communication highlighted the regional commissioning policy for the medicine agreed with local commissioners in July and described the differences in funding sources due to existing contractual arrangements. This email was not provided. The Panel further noted Sanofi's submission that there was evidence that the clarity around contractual arrangements referred to by the complainant did not exist.

The Panel noted that the specialist commissioning group policy document referred to and submitted by Sanofi was effective from 22 July 2011. However the recommended implementation date was noted on the document as 'TBC'. The section entitled 'Financial Implications (PCTs)' stated:

> 'Estimated cost per patient is £10-£20,000 depending on duration of treatment.
> The financial implications are likely to be different dependent upon the provider. Currently there are significant differences in the prices that commissioners pay for bone marrow transplants (BMTs) to different providers. A sub-group of the BMT expert panel is working to determine actual costs. Plerixafor has been introduced during 2010/11 and providers have maintained that it is not included in the locally agreed tariff for the service. Consequently some providers have made IFR requests which have been funded by PCTs.'

The evidence to support Sanofi's submission about the lack of clarity around contractual arrangements included an extract from the minutes of the regional cancer network pharmacists group which referred to three issues with plerixafor. It did not mention what the problems were other than patients were being denied medicines. An email from the cancer network pharmacist to the oncology commissioning representative at Sanofi in March 2012 was also provided. This stated:

> 'What is clear is that commissioners in [the strategic health authority] commission it, our commissioners say that they already pay [the trust] for it, and [the trust] dispute this. In addition it appears that Trusts outside of [the local trust] who are asked to administer it should not go to their PCTs with IFRs or policy requests for funding (as its commissioned) and should instead ask [the trust] to either provide the vials or the money to procure the drug. [The trust] dispute this. This means we are gong round in circles that only the [specialist commissioning group] can stop'

Sanofi also provided a number of emails between the representative in question and clinicians based in the region. All the emails appeared to be in relation to the whether regional funding of Mozobil had been agreed. The representative's emails were sent in October/November 2011. Two responses received by the representative in October 2011 stated, *et al*:

> 'In theory we can apply by IFR, no patient to test on yet.'

And:

> 'The funding is still very up in the air, I did try to clarify, but was told that I had to speak to local managers, but they say to speak to commissioners?! So still not clear.
>
> Certainly we can apply via IFR, but unclear if our local managers will allow treatment at risk.'

A further email, received in November in response to the representative in question stating that she understood that the PCTs in the region had been informed that Mozobil funding was available for patients, read, *et al*:

> 'Sadly this is not the case for the region, though is the case for some parts of the region. There is still significant issue over funding for [the region]. It is still under discussion.'

The Panel noted that the email provided by the complainant stated, *et al*:

> 'At the minute you can submit an IFR for Mozobil to [PCT] or whichever PCT for your patient and they will approve it, until the [specialist commissioning group] give clarity on which pot of money it will be funded from.'

The Panel considered that the emails received by the representative in response to her enquiries in October and November 2011 indicated that whilst there was some confusion about funding it was possible for clinicians to apply to the relevant PCT for funding for Mozobil.

The Panel considered that, contrary to the complainant's assertion, it was not necessarily inappropriate for the representative to discuss funding issues with health professionals so long as such discussions complied with the Code. However, the Panel was concerned that in relation to the email in question the representative stated that the PCT 'will approve' the IFR. The Panel considered that this was a broad claim and inappropriate as alleged. The email responses submitted by Sanofi from clinicians based in the region indicated that there was no certainty as to whether an IFR would be successful. The representative's email was therefore misleading in that regard and a breach of Clause 7.2 was ruled. It was not the representative's role to reassure health professionals that every request would be funded, nor could she be certain that every request would be funded. The Panel considered that the representative had not maintained a high standard of ethical conduct and a breach of Clause 15.2 was ruled.

Complaint received **18 April 2012**

Case completed **22 June 2012**

CASE AUTH/2500/4/12

ANONYMOUS v EISAI

Promotion of Zonegran

An anonymous consultant neurologist alleged that Zonegran (zonisamide) promotional materials, used by a representative of Eisai were misleading. Zonegran was indicated in the treatment of adults with partial seizures. The complainant stated that the materials and discussion with the representative incorrectly inferred that Zonegran could be used in overweight epileptics. The complainant subsequently discovered that weight loss could be a side effect of treatment.

The detailed response from Eisai is given below.

The Panel noted that the complainant was anonymous and non-contactable. A complainant had the burden of proving his/her complaint on the balance of probabilities and all complaints were judged on the evidence provided by the parties. It was impossible to know what the representative had said or what materials he/she had used. The company could not identify the representative in question. The Panel noted that according to Eisai a detail aid was to be used and it thus considered the complainant's allegations solely in relation to that.

The Panel noted that the Zonegran summary of production characteristics (SPC) stated that Zonegran might cause weight loss.

The Panel noted Eisai's submission that as there was similar efficacy between different anti-epileptic medicines other important factors were taken in to account before such medicines were prescribed.

The first page of the Zonegran detail aid gave details of the indication then in larger type the claim 'Think beyond efficacy … When looking for additional seizure control …'. The third page of the detail aid contained four text boxes with the following statements: 'What about side effects?'; 'Will they be able to stay on treatment?'; 'What happens if they forget a dose?' and 'Will it impact on other treatments?'. The detail aid then went on to address these questions. The 'What about side effects?' section listed treatment emergent adverse events reported by ≥10% Zonegran patients. Weight loss was not mentioned. The final section started on page 12 with two pages answering the question 'Will weight gain be an issue?'. This section was separate from that addressing side effects and consisted of the results from Wellmer *et al* (2009) (which looked at the impact of Zonegran on body mass index), details on the issue of weight gain in epileptic patients and the lack of weight gain seen with Zonegran. The fifth and final bullet point was in bold type and stated 'BMI decrease was significant in patients who were overweight prior to Zonegran initiation'.

The Panel noted that the representative briefing document on Wellmer *et al* stated 'In this retrospective study, zonisamide reduced weight in 35% of patients, particularly those who were overweight prior to treatment. This study helps provide some information regarding the variability and extent of weight change under zonisamide treatment in daily practice, however provides no indication of why patients change weight'. This was followed by bold text which read 'Please note that this is a study in epileptic patients on Zonegran & is not advocating the use of Zonegran as a weight loss drug'.

The Panel noted that in describing the study limitations, Wellmer *et al* noted that the retrospective design did not allow controlling variables such as intended weight loss through fasting. It suggested that prospective studies should be carried out. The discussion section noted that weight loss was not restricted to overweight patients and in normal and underweight patients it could be an adverse event. Although weight loss was described as mild to moderate in most cases, in some individuals it reached critical dimensions.

The Panel considered that the detail aid encouraged prescribers to consider factors other than seizure control when deciding which treatment to prescribe. This was not necessarily unacceptable as factors such as side effects would be relevant to the prescribing decision. However the licensed indication should be clear and overall the discussion of factors other than seizure control should be presented in the context of the indication. By separating in the detail aid the weight loss seen with Zonegran from other side effects, the detail aid might imply that Zonegran's indications included weight loss in epileptic patients. This impression was compounded by the fact that there was no mention, other than in the prescribing information, that anorexia was a common side effect. It was not sufficiently clear from the Wellmer *et al* briefing document or the detail aid that the medicine should not be promoted to aid weight loss in epileptic patients. In addition, there was no mention of the study limitations or that it was a retrospective study. There was no briefing material for the detail aid. This was unacceptable.

The Panel considered that, taking all the circumstances into account, the detail aid was misleading with regard to Zonegran's effect on weight loss, and a breach was ruled. The Panel considered that by failing to be clear about Zonegran and weight loss in epilepsy, the detail aid exaggerated the medicine's properties. A breach was ruled. The Panel considered that Eisai had not maintained high standards and a breach was ruled.

The Panel noted its rulings above and considered that, taking all the circumstances into account, they did not warrant a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such use.

The Authority received a complaint from an anonymous consultant neurologist; no contact details were provided. The complaint was about the promotion of Zonegran (zonisamide) by Eisai Limited. Zonegran was indicated in the treatment of adults with partial seizures.

COMPLAINT

The complainant alleged that a representative showed him/her promotional materials which he/she considered were misleading and could endanger patients. The materials and discussion inferred that Zonegran could be used in overweight epileptics. The complainant subsequently discovered that such a suggestion was not evidence based and weight loss could be a side effect of treatment. The complainant noted that a claim could not be made about a side effect as the study was not powered to do this – the study would look at the efficacy of the medicine and an overall safety profile. The complainant alleged that the material and verbal claims were incorrect. The complainant also noted that diarrhoea was a side effect and queried whether he/she should use Zonegran in epileptic patients who were also constipated.

When writing to Eisai, the Authority asked it to respond in relation to Clauses 2, 7.2, 7.10 and 9.1 of the Code.

RESPONSE

Eisai explained that as there was similar efficacy between different anti-epileptic medicines (which was well established for Zonegran which had been on the market for seven years), epileptologists and neurologists considered other important factors such as dosing frequency, interactions with other medicines, tolerability and side effects in order to prescribe an anti-epileptic medicine to match individual patient needs.

With this in mind the detail aid was specifically devised to address questions that might come up during a call with a representative (Eisai provided a copy of the detail aid relevant to the complaint and also the efficacy leavepiece).

The current detail aid was an interactive iPad version, designed such that representatives could bring up specific information, if and when needed, to address prescribers' questions. An identical paper version was used that was replaced with the electronic version in April 2011.

The e-detail addressed a number of prescribers' issues when selecting anti-epileptic medicine treatment such as; frequency of dosing, retention rates on Zonegran, tolerability, reasons for discontinuing treatment with Zonegran, common adverse events with Zonegran, drug-drug interactions with other anti-epileptic medicines or the oral contraceptive pill as well as weight changes with Zonegran. This was a common subject matter as some anti-epileptic medicines might contribute to weight gain whilst others might have minimal effect on weight or a slight weight reduction.

As there were minimal trials published on this matter, the e-detail contained the results from Wellmer *et al* (2009) which looked at the variability and extent of weight change with Zonegran. The result of the study (figure 2 from the published paper) was shown in the e-detail. Thus if a clinician had a question about weight changes on Zonegran, the representative could provide some information about the variability of weight change from a study that investigated this particular topic.

The majority of patients on Zonegran did not experience weight gain, however some patients had weight loss that was reversible following discontinuation of Zonegran and was not related to the dose of Zonegran. This was similar to the result seen in a pivotal Phase III trial (data on file) which was also referenced in the e-detail.

Eisai stated that its representatives had been briefed on each of the studies cited in the e-detail including Wellmer *et al* (a copy of an email and briefing document were provided). The sales team had been clearly told that Wellmer *et al* might explain some of the variability observed with weight changes on Zonegran treatment and that Zonegran must not be promoted as a weight loss agent.

Eisai submitted that there appeared to be a misinterpretation by the complainant who stated that the study should look at efficacy and was not 'powered to detect side effects'. This was not the purpose of the study. The study did not look at efficacy but focused specifically on the impact on weight from observing the effect of Zonegran on 103 epileptic patients.

Eisai stated that the e-detail was intended to clarify issues and present the facts. There was nothing in the material that promoted the use of Zonegran for weight management. Eisai considered that its material was balanced, up-to-date, could be substantiated and did not mislead. The information on the various topics was presented objectively thus the company denied any breaches of Clauses 7.2 and 7.10. In addition, the company denied that the material demonstrated that high standards had not been maintained (Clause 9.1) or that it had reduced confidence in the pharmaceutical industry (Clause 2).

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. A complainant had the burden of proving his/her complaint on the balance of probabilities and all complaints were judged on the evidence provided by the parties. It was impossible to know what the representative had said at the interview and equally impossible to know

what materials he/she had used. The company could not identify the representative in question. The Panel noted that according to Eisai a detail aid was to be used and it thus considered the complainant's allegations solely in relation to the detail aid (ref Zonegran-UK2375a).

The Panel noted that the allegation concerned a discussion about the use of Zonegran for weight loss for epileptic patients who were overweight, when in fact weight loss was a side effect for the medicine, not an indication. The Panel noted Section 4.4, Special warnings and precautions for use, of the Zonegran SPC, stated that Zonegran might cause weight loss. If substantial undesirable weight loss occurred discontinuation of Zonegran should be considered. Section 4.7, Undesirable effects, listed anorexia as very common (≥1/10) and weight decrease as common (≥1/100<1/10). The SPC stated that the most common adverse reactions in controlled adjunctive therapy studies were somnolence, dizziness and anorexia.

The Panel noted Eisai's submission that as there was similar efficacy between different anti-epileptic medicines, epileptologists and neurologists took other important factors into account before prescribing such medicines.

The first page of the detail aid provided by Eisai gave details of the indication then in larger type the claim 'Think beyond efficacy ... When looking for additional seizure control ...'. The brand name 'Zonegran' appeared at the bottom right corner of this page, below which was the strap line 'Beyond efficacy'. The third page of the detail aid contained four text boxes with the following statements: 'What about side effects?'; 'Will they be able to stay on treatment?'; 'What happens if they forget a dose?' and 'Will it impact on other treatments?'. The detail aid then went on to address these questions. The 'What about side effects?' section listed treatment emergent adverse events reported by ≥10% Zonegran patients in Brodie *et al* (2005). Weight loss was not mentioned. The final section started on page 12 with two pages answering the question 'Will weight gain be an issue?'. This section was separate from that addressing side effects and consisted of one page showing the results from Wellmer *et al*, which looked at the impact of Zonegran on body mass index (BMI), and a second page with the sub heading 'The majority of patients treated with Zonegran did not experience weight gain'. This page then had four bullet points detailing the issue of weight gain in epileptic patients and the lack of weight gain seen with Zonegran. The fifth and final bullet point was in bold type and stated 'BMI decrease was significant in patients who were overweight prior to Zonegran initiation'. This was also referenced to Wellmer *et al*.

The Panel noted that the representatives' briefing document on Wellmer *et al* (ref Zonegran-UK2373) had the same title as the paper, 'The impact of zonisamide on weight. A clinical study in 103 patients with epilepsy' and was labelled '(internal use only)'. It covered the objective, design, results and conclusion of the study. Wellmer *et al* did not mention the type of epilepsy and as noted in the briefing material it was possible that some patients were outside the Zonegran indication. The conclusion noted on the briefing document stated 'In this retrospective study, zonisamide reduced weight in 35% of patients, particularly those who were overweight prior to treatment. This study helps provide some information regarding the variability and extent of weight change under zonisamide treatment in daily practice, however provides no indication of why patients change weight'. This was followed by bold text which read 'Please note that this is a study in epileptic patients on Zonegran & is not advocating the use of Zonegran as a weight loss drug'. There was then further bold text in a box which stated 'This article is for your information and is not to be distributed proactively. Should you receive a request for a copy of this article, please contact Medical Information'. There did not appear to be a briefing document for the detail aid.

The Panel noted that in describing the study limitations, Wellmer *et al* noted that the retrospective design did not allow controlling variables such as intended weight loss through fasting. It suggested that prospective studies should be carried out. The discussion section noted that weight loss was not restricted to overweight patients and in normal and underweight patients it could be an adverse event. Although weight loss was described as mild to moderate in most cases, in some individuals it reached critical dimensions. The Phase III study, Zonegran 302c, looked at the safety and efficacy of Zonegran. The extract (dated 2005) provided by Eisai concluded that 'There were no marked changes in mean weight in any of the zonisamide or placebo treatment groups. Slightly larger decreases were seen with zonisamide compared with placebo, although the overall effect on weight loss was considered to be mild. There was no evidence to suggest that the weight loss was associated with the dose of zonisamide'. This also stated that weight loss (less than 10%) was more frequent in treated patients (5%, n=498) than placebo (1.7%, n=350).

The Panel considered that contrary to the complainant's allegation Eisai had some data about weight loss in a study which looked specifically at this aspect.

The Panel considered that the theme of the detail aid encouraged prescribers to consider factors other than seizure control when deciding which treatment to prescribe for patients who needed adjunctive therapy. This was not necessarily unacceptable as factors such as side effects would be relevant to the prescribing decision. However the licensed indication should be clear and overall the discussion of factors other than seizure control should be presented in the context of the indication. By separating in the detail aid the weight loss seen with Zonegran from other side effects, the detail aid might give the impression that Zonegran's indications included weight loss in epileptic patients. This impression was compounded by the fact that there was no mention, other than in the prescribing

information, that anorexia was a common side effect and that the weight gain section was the final one in the detail aid and therefore likely to be the last topic the representative discussed with a health professional before closing the call. Although the statement at the end of the briefing document for Wellmer *et al* emphasised that Zonegran was not a weight loss medicine, it was not sufficiently clear from the Wellmer *et al* briefing document or the detail aid that the medicine should not be promoted to aid weight loss in epileptic patients. Representatives needed very clear, unambiguous guidance in this regard. The Panel was also concerned about the claims in the detail aid referenced to Wellmer *et al*. There was no mention of the study limitations or that it was a retrospective study. There did not appear to be any briefing material for the detail aid. This was unacceptable.

The Panel considered that, taking all the circumstances into account, the detail aid was misleading with regard to Zonegran's effect on weight, and a breach of Clause 7.2 was ruled. The Panel considered that by failing to be clear about Zonegran and weight loss in epilepsy, the detail aid exaggerated the medicine's properties. A breach of Clause 7.10 was ruled. The Panel considered that Eisai had not maintained high standards and a breach of Clause 9.1 was ruled. The Panel noted its rulings above and considered that, taking all the circumstances into account, they did not warrant a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such use. No breach of Clause 2 was ruled.

Complaint received **20 April 2012**

Case completed **20 June 2012**

CASE AUTH/2503/5/12

GENERAL PRACTITIONER v GENUS

Promotion of Cetraben

A general practitioner alleged that an advertisement for Cetraben, issued by Genus, was offensive and degrading due to its sexual and titillating picture. Cetraben was an emollient used particularly for symptomatic relief in eczema.

The advertisement featured the back view of a young woman walking down a city street. The wind appeared to have lifted her short turquoise skirt to reveal red and white polka dot underwear. The photograph showed her looking over her left shoulder and gasping. The headline read: 'Confidence to live life their way*' followed beneath by '*However that might be'. The complainant stated that he despaired of the industry's standards and culture that such an advertisement should be considered appropriate.

The detailed response from Genus is given below.

The Panel noted the Code required materials and activities to recognise the special nature of medicines and the professional standing of the audience and not be likely to cause offence. Supplementary information stated that the display of naked or partially naked people for the purpose of attracting attention and the use of sexual imagery for that purpose was unacceptable.

The Panel recognised that eczema might affect a patient's self esteem and confidence and noted Genus' submission that the advertising campaign was developed specifically to acknowledge the potential negative effects of eczema on people's lives and demonstrate the positive impact successful treatment could have by restoring self confidence.

Turning to the advertisement in question, the Panel considered that 'confidence' could have been portrayed in other ways. The Panel considered that the suggestive manner in which the young woman's underwear was exposed was for the purpose of attracting attention to the advertisement, rather than to show the impact of the treatment on a patient's confidence. The Panel considered that the material did not recognise the special nature of medicines and the professional standing of the audience to which it was directed and was likely to cause offence. A breach of the Code was ruled.

A general practitioner complained about an advertisement for Cetraben (white soft paraffin, light liquid paraffin) (ref CET04121348B) issued by Genus Pharmaceuticals published in GP, 25 April 2012. Cetraben was an emollient used particularly for symptomatic relief in eczema. The advertisement featured the back view of a young woman walking down a city street. The wind appeared to have lifted her short turquoise skirt to reveal red and white polka dot underwear. The photograph showed her looking over her left shoulder and gasping. The headline read: 'Confidence to live life their way*' followed beneath by '*However that might be'.

COMPLAINT

The complainant alleged that the advertisement was offensive and degrading due to its sexual and titillating picture. The complainant stated that he despaired of the industry's standards and culture that such an advertisement should be considered appropriate.

When writing to Genus, the Authority asked it to consider the requirements of Clause 9.2 of the Code.

RESPONSE

Genus submitted that the Cetraben campaign had been developed to reflect a number of important treatment needs for patients with eczema. There were currently over 6 million patients in the UK who suffered from dry skin or eczema and the incidence of eczema had increased by 42% between 2001 and 2005. The effects of eczema were manifold and if not treated effectively could result in a number of distressing sequelae including depression, anxiety, major sleep disturbance, bullying and difficulty socialising.

Genus submitted that the effect of eczema on individuals' self-esteem and self-confidence was a major consideration. Thirty six percent of people with eczema reported that the condition could affect their self-confidence and 43% were concerned about being seen in public while suffering an exacerbation of eczema.

Genus stated that the Cetraben campaign was developed specifically to acknowledge these potential negative effects of eczema on people's lives and demonstrate the positive impact that successful treatment could have in allowing patients to continue with normal activity and removing the detrimental effect on self-confidence – hence the headline 'Confidence to live life their way'.

Genus explained that eczema affected people of all ages. The Cetraben campaign recognised three major demographics: young children, women and the elderly. Eleven percent of eczema patients were under 12 years, 47% were between 13 and 55 and 42% were over 56. The advertising campaign comprised three separate creative treatments each of which addressed one of these age demographics (copies of the advertisements were provided). Equal emphasis had been placed on each of these age groups within the campaign.

Genus noted that the complainant had cited only one of the age groups – the younger female. Genus explained that young women with eczema were a group of patients whose requirement for effective treatment had increased significantly over the past few years and who had particular requirements from their treatment. Eczema was more common in women than in men except in those under 5 and over 80. This difference in prevalence between the sexes was seen mostly in the ages of 20 to 40 when the prevalence in females was over twice that in males. GP consultations for eczema were proportionately much higher for women between 20 and 40 than for men – a difference that only evened out when patients reached their 70s and 80s when the consultation rates for men and women were comparable. The Cetraben advertising campaign reflected this situation.

Genus noted that the complaint was about the advertisement which featured a young woman and so it assumed that the complainant had not seen or chose not to complain about the three older female patients who were shown in bathing suits, although it acknowledged that the complainant might not yet have seen the other advertisements.

Genus submitted that the advertisement at issue was developed in response to the growing number of young women with eczema who presented to GPs nationwide. A key issue for these patients was being seen in public when they were suffering an eczema exacerbation; 46% of females with eczema were concerned about being seen in public. It was this effect on patients' quality of life that was addressed in the Cetraben campaign. Indeed it was most often the everyday activities depicted that patients avoided; 86% of patients avoided at least one type of everyday activity while in flare - these include bathing, wearing shorts, skirts or T-shirts and swimming.

Genus stated that, in summary, as Cetraben was indicated for the treatment of dry skin and eczema it was inevitable that promotional imagery should depict naked skin and that this was consistent with advertising for other dermatological conditions. Genus noted that other medicines had promoted dermatological brands with a significantly higher degree of nakedness than was used in the Cetraben advertisement now at issue all of which featured people in everyday clothing none of which could be described as skimpy.

Genus noted that similar issues regarding dermatological products were addressed by the PMCPA on a number of occasions, most recently in Case AUTH/2304/3/10 in which the promotion of Exorex lotion featured a women in her underwear walking though a supermarket. Breaches of Clauses 9.2 and 9.1 were considered but the Panel considered the imagery relevant to the therapeutic area.

The Cetraben campaign was a light-hearted route to engage health professionals in what was a serious matter for eczema patients and it showed the positive impact on self-esteem and self-confidence brought about by successful treatment.

Genus submitted that the woman photographed was only embarrassed that her skirt had blown up in the wind – to demonstrate that because of successful treatment of her eczema she now had the confidence to wear a skirt and not cover her legs.

Genus considered that the Cetraben campaign was an appropriate way to depict the positive benefits of effective treatment. There was both a strong medical and a marketing rationale to present patients in the way it had. The advertisements depicted patients that would be readily recognised by health professionals who routinely treated eczema patients of these types. Genus considered that the advertisements successfully promoted Cetraben and the need for effective treatment of a condition that could otherwise have a serious and negative effect on patients' quality of life.

Genus stated that it took Clause 9 into account when it drew up the advertisement and it was mindful of the clause criteria and judged the advertisement in light of similar promotional pieces seen throughout the health professional environment. In Genus's view the advertisement conveyed the message intended in a non-sexual manner.

Genus noted that subjectivity of an audience was difficult to measure and it believed strongly it was aligned with the type of images commonly used within the industry for dermatology products and was not in breach of Clause 9.2.

PANEL RULING

The Panel noted the requirement of Clause 9.2 that materials and activities must recognise the special nature of medicines and the professional standing of the audience and must not be likely to cause offence. The supplementary information to Clause 9.1 and 9.2 stated that the display of naked or partially naked people for the purpose of attracting attention and the use of sexual imagery for that purpose was unacceptable.

The Panel noted Genus' submission that the advertisement in question was one of three which featured three major eczema demographics; younger children, female adults and the elderly.

The Panel recognised that eczema might affect a patient's self esteem and confidence and noted Genus' submission that the advertising campaign was developed specifically to acknowledge the potential negative effects of eczema on people's lives and demonstrate the positive impact successful treatment could have by restoring self confidence.

The Panel noted Genus' submission that promotional imagery for a treatment for dry skin and eczema would inevitably depict naked skin. The Panel considered that whilst depiction of naked skin was not necessarily unacceptable it must comply with the Code, in particular the supplementary

information to Clauses 9.1 and 9.2, Suitability and Taste, which stated, *et al*, that the display of naked flesh for the purpose of attracting attention to the material or the use of sexual imagery for that purpose were unacceptable styles of promotion.

Turning to the advertisement in question, the Panel considered that 'confidence' could have been portrayed in other ways for example by showing the young woman's legs without exposing her underwear. The Panel considered that the suggestive manner in which her underwear was exposed was for the purpose of attracting attention to the advertisement, rather than to show the impact of the treatment on a patient's confidence. The Panel noted the supplementary information to Clause 9.1 and 9.2, Suitability and Taste, as set out above and considered that, consequently, the material thus did not recognise the special nature of medicines and the professional standing of the audience to which it was directed and was likely to cause offence. A breach of Clause 9.2 was ruled.

Complaint received **3 May 2012**

Case completed **2 July 2012**

ANONYMOUS v PROSTRAKAN

Promotion of Abstral

An anonymous non-contactable complainant who worked in a specialist burns unit alleged that a medical liaison specialist from ProStrakan had promoted the off-label use of Abstral (fentanyl) sub-lingual tablets. Abstral was indicated for the management of breakthrough pain in adults who used opioids for chronic cancer pain.

The complainant explained that he/she had recently been visited by a ProStrakan employee whom he/she agreed to see only because the employee claimed to be an medical liaison specialist (not a sales representative). The complainant stated that he/she was surprised when the company representative did not show any off label data at all; the only data the complainant was shown related to studies in breakthrough cancer pain when patients were otherwise controlled on a background of around the clock sustained release morphine or equivalent.

The complainant stated that the medical liaison specialist continued to question him/her and it soon became clear that the medical liaison specialist was interested in the complainant's prescribing of fentanyl lozenges [Actiq marketed by Cephalon]. The speed of action of the two medicines was compared relating this to dressing changes or movement. The complainant asked for supporting data but none was forthcoming. The complainant assumed that there was no data in this cohort of patients.

If companies discussed off-licence use they should at least have some off-licence data. As far as the complainant could establish, the medical liaison specialist had no medical training and no off-licence data. The complainant considered that the medical liaison specialist's conduct was a flagrant attempt to widen the prescribing of Abstral.

The detailed response from ProStrakan is given below.

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

The Panel considered that companies had to be extremely careful in ensuring that their medicines were not promoted for unlicensed indications. The role of MLE staff and the like needed to be very carefully controlled with detailed instructions. Guidance in this regard had recently been published in the PMCPA guidance on Clause 3 of the Code.

The Code defined a representative as anyone calling on members of the health professions and administrative staff in relation to the promotion of medicines. This was a wide definition and could cover the activities of those employees that companies might not call representatives. The Code defined 'promotion' as 'any activity undertaken by a pharmaceutical company or with its authority which promotes the prescription, supply, sale or administration of its medicines'.

The Panel noted that the parties' accounts differed. The complainant stated that he/she had agreed to see a medical liaison executive (MLE) who showed him/her data relating to studies in breakthrough cancer pain and was interested in his/her prescribing of a competitor medicine in the specialist burns unit. The MLE compared the two medicines in relation to speed of action and related this to dressing changes and movement. The complainant alleged that the MLE had no data to support the use of Abstral in this cohort of patients. ProStrakan had submitted that its procedures only permitted MLEs to interact with burns units following an unsolicited request for information from that individual. Proactive, routine and unsolicited discussion of the off-label use of Abstral was prohibited by ProStrakan. ProStrakan had also submitted that the MLE team did not discuss both licensed and unlicensed use of Abstral in the same call. If a health professional asked an unsolicited question about the licensed use of Abstral during a discussion of off-licence use the MLE would answer that question.

The Panel further noted ProStrakan's submission that between February 2011 and May 2012 its MLE team had received only three requests relating to the use of Abstral in burns patients. In all cases these interactions had been prompted by requests for information by the health professional.

The Panel noted ProStrakan's submission that its MLE team was a field based extension of its medical information function. On reviewing the MLE job description, the Panel noted the role was split into two, a reactive part (referred to in ProStrakan's response) and a proactive part which was made up of two functions; firstly to engage with stakeholders regarding within licence scientific data in a balanced, non-promotional way and secondly to proactively contact external stakeholders in relation to scientific publication, clinical studies, disease awareness and non promotional new data. To this extent, the Panel considered that this role went beyond that of a medical information department. The Panel further

noted the informal guidance on Clause 3 of the Code issued by the Authority.

The Panel thus considered that one aspect of the MLE role as described in the job description was likely to involve the promotion of ProStrakan medicines. In the Panel's view the job description meant that MLEs would call proactively on health professionals and this may have included the call upon the complainant. ProStrakan had not commented on the discussion regarding fentanyl lozenges.

The Panel considered that the parties' accounts differed and it was not possible to determine where the truth lay. On the very limited information provided by the complainant it was not possible for ProStrakan to identify the MLE/representative involved. It was not possible to contact the complainant for more information. The Panel considered that the complainant had not established his/her case on the balance of probabilities. No breach of the Code was ruled including no breach of Clause 2.

An anonymous non-contactable complainant alleged that a medical liaison specialist from ProStrakan had promoted the off-label use of Abstral (fentanyl) sub-lingual tablets. Abstral was indicated for the management of breakthrough pain in adults who used opioids for chronic cancer pain.

COMPLAINT

The complainant explained that he/she had recently been visited by a ProStrakan employee whom he/she agreed to see only because the employee claimed to be an medical liaison specialist (not a sales representative). The complainant explained that he/she worked in a specialist burns unit and needed a portfolio of pain medicines.

The complainant stated that he/she was surprised when the company representative did not show any off label data at all; the only data the complainant was shown related to studies in breakthrough cancer pain when patients were otherwise controlled on a background of around the clock sustained release morphine or equivalent.

The complainant stated that the medical liaison specialist continued to question him/her and it soon became clear that the medical liaison specialist was interested in the complainant's prescribing of fentanyl lozenges [Actiq marketed by Cephalon]. The speed of action of the two medicines was compared relating this to dressing changes or movement. The complainant asked for supporting data but none was forthcoming. The complainant could only assume that there was no data in this cohort of patients.

The complainant understood that if companies discussed off-licence use they should at least have some off-licence data. As far as the complainant could establish, the medical liaison specialist had no medical training and no off-licence data. The complainant considered that the medical liaison specialist's conduct was a flagrant attempt to widen the prescribing of Abstral.

The complainant questioned the medical liaison specialist as to the validity of his/her conduct and was told that it was endorsed by the company from senior management down and that it was perfectly legitimate. The complainant was also told that a significant UK team had daily discussions as above.

The complainant alleged that use of fentanyl products without the appropriate expertise and knowledge was dangerous, and lethal in the wrong environment. This practice concerned the complainant greatly.

When writing to ProStrakan the Authority asked it to respond in relation to the requirements of Clauses 2, 3.1, 9.1, 15.2 and 15.9.

RESPONSE

ProStrakan explained that its field-based team of medical liaison specialists, called medical liaison executives (MLEs), reactively responded to questions from health professionals about the off-label use of Abstral. The team was an extension of the medical information function and as such reported exclusively to the medical director (latterly to the senior vice president for Northern Europe as the post of medical director was vacant). The MLE team was established to provide balanced, non-promotional, scientific and technical support to those health professionals who requested it.

ProStrakan submitted that MLE activity was wholly separate to that of the promotional sales teams. If a sales representative was asked about the off-label use of ProStrakan's products he or she might pass this on to the MLE team, but responses to such questions must be completed and delivered by the MLE team through appropriate and separate non-promotional channels.

ProStrakan explained that its procedures only permitted MLEs to interact with health professionals in burns units if they had an unsolicited request for information from that individual. Proactive, routine and unsolicited discussion of the off-label use of Abstral was strictly prohibited as this would violate the Code.

ProStrakan noted the allegation that the complainant was proactively contacted by a company employee to discuss the off-label use of Abstral. This was a serious allegation and as such ProStrakan hoped to be able to investigate the matter further but the lack of detail from the anonymous complainant and the fact that the complainant could not be contacted for further information, meant that it was difficult to fully investigate the complaint. Furthermore, there was no hint at the geographical location of the complainant that would help to focus any further investigations.

ProStrakan submitted that its investigations showed that between February 2011 and May 2012 the MLE team received 432 requests to respond to health

professionals about the use of its products. Of these, three requests were about the use of Abstral in burns patients and all had been prompted by requests from the health professional for information as described above.

ProStrakan was assessing an investigator sponsored trial (IST) proposal submitted by a physician who worked in a burns unit. This proposal, which included off-label use of Abstral, was first discussed with an MLE who helped the individual in question to prepare the application now being considered by the ProStrakan IST committee. ProStrakan reiterated that this study proposal was initiated by the health professional concerned.

ProStrakan had not sought to extend the marketing authorization for Abstral to include burns patients.

ProStrakan submitted that the MLEs did not discuss both the licensed and unlicensed use of Abstral in the same call. The MLE team had been trained to respond only to the specific question asked by a health professional with regard to off-label use, so as not to provide any further detail on topics not mentioned in the original request and that might be construed as promotional.

ProStrakan noted that its MLEs had been interviewed and asked if they discussed both licensed and unlicensed use of Abstral in the same call. Their responses reflected the training that they received. However, it was noted that customers had, on occasion, asked for the licensed indications of Abstral to be clarified while they discussed the original off-label question. In such instances the MLE would provide the information sought, but only after they had reiterated the non-promotional nature of their role to the health professional concerned.

ProStrakan noted that no training materials, briefing documents or any other items had been produced for the MLE team that discussed the use of Abstral in burns patients.

In conclusion, given their status as an extension of the medical department, and the fact that their activity with regard to the discussion of off-label product use was reactive only, ProStrakan maintained that its MLE function was as a field-based, non-promotional medical information service, an activity which was entirely distinct and different to that provided by the sales team. While MLEs engaged in off-label discussions with health professionals, these discussions were entirely at the request of the health professionals in question and maintained a high standard of ethical conduct that complied with all relevant requirements of the Code. As such ProStrakan did not believe that Clauses 3.2 or 15.2 had been breached. As there were no MLE materials of any description that discussed or advocated the use of Abstral in burns patients, either directly or indirectly, ProStrakan did not consider that Clause 15.9 had been breached.

ProStrakan stated that its MLE team was established to provide a scientific service to the medical community and that it had appropriate training and procedures to ensure that the service was provided in an ethical and compliant fashion. The company therefore submitted that high standards had been upheld; no breach of Clause 9.1 had occurred and consequently a ruling of a breach of Clause 2 was not justified.

ProStrakan submitted that although it respected the anonymity of the complainant, that anonymity not only limited the company's ability to investigate the allegations in more detail, but it also deprived the company of the standard reassurances provided by the PMCPA that the complainant had been asked to declare any conflict of interest. In that regard ProStrakan noted that one of its MLEs had recently been dismissed, although not for issues relating to performance or compliance.

Following a request for further information, ProStrakan submitted that the MLEs were expected to proactively stay abreast of developments in the scientific field in which they were working. It was anticipated that they would be aware of new data and publications in the relevant therapy area, including disease-specific and therapy-specific publications and guidelines, and that they would share this information with their colleagues in the medical department so that any information exchange and information updates could be internally coordinated.

ProStrakan stated that while the MLE job description mentioned that the team might provide 'proactive customer support' there had not yet been an occasion where such proactive contact has been necessary. If this were to occur in the future then any 'proactive customer support' would be in relation to the exchange of 'within licence' scientific data in a balanced, non-promotional manner and not in conjunction with any promotional-related person or strategy, eg to make customers aware of emergent phase IV data for Abstral within its licensed indication.

ProStrakan submitted that the MLE team was re-interviewed as a consequence of the PMCPA's request for further information. The responses given by all team members during these interviews consistently backed-up the description given above in relation to providing proactive support.

ProStrakan confirmed that MLEs did not proactively mention or discuss competitor products with health professionals. If during a call with a health professional the subject of competitors was raised by the health professional, the MLE would briefly answer any questions they were specifically asked, but point out that promotional discussions would have to be held with a sales representative from the company. They would then offer to arrange for the health professional to be contacted by the appropriate sales representative at a future date.

ProStrakan submitted that the key data relating to the onset of action of Abstral came from Rauck *et al* (2009). This was a randomised, placebo-controlled

trial in 131 opioid-tolerant patients with breakthrough cancer pain. Sixty one patients were assessed for efficacy at 10 minute intervals over a 60 minute period. Pain intensity difference (PID) was calculated by comparing pain intensity scores (rated from 0-10, where 0 is 'no pain' and 10 is 'pain as bad as you can imagine') at baseline and after treatment. Significant improvements in PID were seen from 10 minutes with Abstral vs placebo. Additionally, significant improvements in PID were maintained throughout the 60 minute assessment period. These findings were consistent with the description of the pharmacodynamic properties of Abstral in section 5.1 of the Abstral summary of product characteristics (SPC).

ProStrakan stated that the key data relating to the onset of action for Actiq came from Coluzzi *et al* (2001). This was a double-blind, double-dummy, randomised, multiple cross-over study conducted in 134 adult ambulatory cancer patients. Patients received medication to target episodes of breakthrough cancer pain, comprising either titrated doses of Actiq paired with placebo capsules or morphine sulfate immediate release (MSIR) capsules paired with placebo lozenges. Efficacy assessment conducted at 15, 30, 45 and 60 minutes showed mean pain intensity scores were significantly better with Actiq than MSIR at all time points and mean pain intensity difference scores also favoured Actiq at all time points. Actiq also demonstrated significantly higher pain relief scores than MSIR at all time points. Of patients opting to enrol in an open-label follow-on study, 94% chose to continue with Actiq, compared to 6% opting for MSIR. The authors concluded that Actiq was more effective than MSIR in treating breakthrough cancer pain. Again these findings were entirely consistent with the description of the pharmacodynamic properties of Actiq outlined in section 5.1 of the Actiq SPC.

ProStrakan stated that there were no head to head studies comparing the onset of action of Abstral v Actiq. As part of their initial training and induction programme the MLE team had been fully trained on the onset of action data outlined above for both Abstral and Actiq.

ProStrakan submitted that its internal records showed that no proactive contact had been made between MLEs and health professionals between February 2011 and May 2012. All contact between MLEs and health professionals that occurred since the team's inception in February 2011 had been as a response to an unsolicited request received from a health professional.

PANEL RULING

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

The Panel considered that companies had to be extremely careful in ensuring that their medicines were not promoted for unlicensed indications. The role of MLE staff and the like needed to be very carefully controlled with detailed instructions. Guidance in this regard had recently been published in the PMCPA guidance on Clause 3 of the Code.

The Code defined a representative in Clause 1.6 as anyone calling on members of the health professions and administrative staff in relation to the promotion of medicines. This was a wide definition and could cover the activities of those employees that companies might not call representatives. Clause 1.2 defined 'promotion' as 'any activity undertaken by a pharmaceutical company or with its authority which promotes the prescription, supply, sale or administration of its medicines'.

The Panel noted that the parties' accounts differed. The complainant stated that he/she had agreed to see an MLE who showed him/her data relating to studies in breakthrough cancer pain and was interested in his/her prescribing of a competitor medicine (fentanyl lozenge (Actiq) produced by Cephalon) in the specialist burns unit. The MLE compared the two medicines in relation to speed of action and related this to dressing changes and movement. The complainant alleged that the MLE had no data to support the use of Abstral in this cohort of patients. ProStrakan had submitted that its procedures only permitted MLEs to interact with burns units following an unsolicited request for information from that individual. Proactive, routine and unsolicited discussion of the off-label use of Abstral was prohibited by ProStrakan. ProStrakan had also submitted that the MLE team did not discuss both licensed and unlicensed use of Abstral in the same call. If a health professional asked an unsolicited question about the licensed use of Abstral during a discussion of off-licence use the MLE would answer that question.

The Panel further noted ProStrakan's submission that between February 2011 and May 2012 its MLE team had received 432 requests to respond to health professionals regarding the use of ProStrakan's products; three of these related to the use of Abstral in burns patients. In all cases these interactions had been prompted by requests for information by the health professional. ProStrakan had stated that it was in the process of assessing a proposal for an investigator sponsored trial submitted by a physician who worked in a burns unit and an MLE had discussed this with the physician and assisted in the preparation of the application to ProStrakan. The study proposal was initiated by the health professional concerned.

The Panel noted ProStrakan's submission that its MLE team was a field based extension of its medical information function. On reviewing the MLE job description, the Panel noted the role was split into

two, a reactive part (referred to in ProStrakan's response) and a proactive part which was made up of two functions; firstly to engage with stakeholders regarding within licence scientific data in a balanced, non-promotional way and secondly to proactively contact external stakeholders in relation to scientific publication, clinical studies, disease awareness and non promotional new data. To this extent, the Panel considered that this role went beyond that of a medical information department. The Panel further noted the informal guidance on Clause 3 of the Code issued by the Authority that stated:

> 'If the medical and scientific liaison executives and the like call upon health professionals and/or appropriate administrative staff to discuss diseases, and there is no reference either direct or indirect to specific medicines, then this activity is covered by an exemption to the definition of promotion given in Clause 1.2 of the Code. This states, *et al*, that the term promotion does not apply to statements relating to human health or disease provided there is no reference either direct or indirect to specific medicines.
>
> If specific medicines are referred to either directly or indirectly, then the activity could not take the benefit of that exemption and could be likely to be seen as promotion of those medicines'.

The Panel thus considered that one aspect of the MLE role as described in the job description was likely to involve the promotion of ProStrakan medicines. In the Panel's view the job description meant that MLEs would call proactively on health professionals and this may have included the call upon the complainant. ProStrakan had not commented on the discussion regarding fentanyl lozenges.

The Panel considered that the parties' accounts differed and it was not possible to determine where the truth lay. On the very limited information provided by the complainant it was not possible for ProStrakan to identify the MLE/representative involved. It was not possible to contact the complainant for more information. The Panel considered that the complainant had not established his/her case on the balance of probabilities. No breach of Clauses 3.2, 9.1, 15.2, 15.9 and 2 was ruled.

During its consideration of this case the Panel further noted ProStrakan's submission that there were no training materials, briefing documents or any other items produced for the MLE team that discussed the use of Abstral in burns patients. However, ProStrakan had also submitted that the MLE team had, between February 2011 and May 2012, responded to three requests from health professionals for information on the use of Abstral in burns patients. The Panel was very concerned that the MLEs had responded to such requests apparently in the absence of any relevant training. The Panel considered that ProStrakan should, as a matter of some urgency, review the role and training provided to MLEs in relation to the requirements of the Code.

Complaint received **10 May 2012**

Case completed **22 June 2012**

ANONYMOUS v PROSTRAKAN

Promotion of Abstral

An anonymous physician alleged that an un-named ProStrakan representative had misled him/her with regard to the titration schedule for Abstral (fentanyl citrate). Abstral was indicated for the management of breakthrough cancer pain (BTcP) in adults using opioids for chronic cancer pain.

The complainant stated that he/she had been shown a document which looked like a prescription record card, but had not been given a copy of it. The complainant stated that the dosing looked simple. On day 1 the dose was 100mcg with a rescue dose of 100mcg. If pain relief was not obtained on day 1, the dose for day 2 should start at 200mcg with a rescue of 100mcg. This dose was used all day on day 2 and day 3 would start with a dose of 300mcg and so on until the right dose was reached.

The complainant stated that as he/she wanted to prescribe Abstral, he/she subsequently looked up the product information on-line and found that the information from the representative was totally different to the approved titration process. This sort of misinformation could affect patient care.

The detailed response from ProStrakan is given below.

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

The Panel noted from the Abstral summary of product characteristics (SPC) that all patients must start therapy with a single 100mcg sublingual tablet. If adequate analgesia was not obtained in 15-30 minutes a second 100mcg tablet could be given. If adequate analgesia was not obtained within 15-30 minutes of the first dose, an increase in dose to the next highest tablet strength should be considered for the next episode of BTcP. Dose escalation should continue in a stepwise manner until adequate analgesia was achieved. The maximum dose for the treatment of any episode of BTcP was 800mcg.

The Panel noted that ProStrakan had provided a copy of the Abstral Titration Chart which it assumed was the document referred to by the complainant. This chart showed that for the first episode of BTcP, patients should be given a 100mcg tablet with the option of a second tablet if the first was not effective after 15-30 minutes. If a second tablet had to be given then treatment of the second episode of BTcP should begin with a 200mcg tablet and the titration schedule continued in this stepwise manner until adequate analgesia or the maximum dose (800mcg) was achieved, whichever came sooner. The Panel noted the layout of the titration chart and queried whether the complainant had mistaken BTcP episodes 1 to 6 with treatment days 1 to 6. In the Panel's view the titration chart was in accordance with the titration schedule contained within the Abstral SPC.

The Panel noted that in training slides 'Abstral:product profile and clinical value' a slide headed 'Titration of Abstral' correctly referred to doses being increased, if necessary, with subsequent episodes of BTcP. Similarly a titration wheel showed that if a rescue dose had been required then the dose of the first tablet should be increased for the next episode of pain.

ProStrakan had not found evidence that any of its staff knew anything about the daily titration schedule referred to by the complainant. All of the materials provided by ProStrakan referred to the dose of Abstral being increased, if necessary, with subsequent episodes of BTcP in accordance with the SPC. On the basis of the information before it, the Panel considered that the complainant had not established, on the balance of probabilities, that a representative had advised him/her to titrate Abstral on a daily basis as alleged. No breach of the Code was ruled.

An anonymous, non-contactable, pain physician, who also managed palliative care patients, complained about what an un-named representative had told him/her about the titration of Abstral (fentanyl citrate). Abstral, marketed by ProStrakan UK Ltd, was indicated for the management of breakthrough pain in adult patients using opioid therapy for chronic cancer pain. The exchange between the complainant and the representative had taken place at a meeting.

COMPLAINT

The complainant stated that he/she had asked the representative about the titration process for Abstral which he/she had heard was difficult. The complainant stated that the representative showed him/her a document which had been developed by a palliative care team in Scotland in collaboration with ProStrakan. The document looked like a prescription record card similar to a cardex system.

The complainant stated that the dosing looked simple. The first dose was the lowest strength of 100mcg with the rescue dose also being 100mcg. This was to be used for all episodes of severe pain on day 1. If pain relief was not achieved on day 1,

the dose for day 2 should start at 200mcg with a rescue of 100mcg. This dose was then used all day on day 2. Day 3 would start at 300mcg with a rescue of another 100mcg and so on until the right dose was reached. The complainant stated that the representative would not give him/her the information to take away because he/she did not have copies to hand out. The complainant considered this looked simple to prescribe and use as he/she could change the prescription each morning depending on how the patient had responded the previous day.

The complainant stated that he/she wanted to try Abstral in his/her next patient. As the information had not been provided to take away the complainant looked up the product information online and saw that the approved titration process was much quicker and did not keep the dosing the same for a full day. The information from the representative was totally different to the approved titration process.

The complainant alleged that this sort of misinformation affected the care of patients and should not be allowed, and he/she would never trust what a representative told him/her again.

When writing to ProStrakan, the Authority asked it to respond in relation to Clauses 2, 3.2, 7.2, 7.4, 9.1, 15.2, and 15.9 of the Code.

RESPONSE

ProStrakan stated that it had conducted a full review of its material which referred to the titration of Abstral and whilst none had matched the complainant's description, the Abstral Titration Chart (ref M017/0476) was identified which, without further information or evidence provided by the complainant, ProStrakan assumed was the item in question.

ProStrakan submitted that the titration chart was produced to assist health professionals with the recommended prescribing of Abstral and the titration in hospitals. The titration schedule in the chart was consistent with the Abstral summary of product characteristics (SPC) and the item was certified before use. It was available for representatives to distribute to health professionals. A copy of the chart was provided.

ProStrakan stated that it took all complaints very seriously and in that regard it had interviewed relevant staff connected to the promotion of Abstral and it became clear that titration was a frequent topic discussed by representatives and health professionals. However, none of the interviewees described a titration schedule that differed from that in the Abstral SPC. At the conclusion of each discussion each interviewee was read the titration schedule detailed in the complaint; none of them had encountered, or knew of, such a titration schedule. Indeed, each interviewee noted the time and care taken to train the teams on the titration process. None of the managers interviewed were concerned about their team's understanding of the Abstral titration process and all asserted that it was an issue that they regularly monitored on field visits. No manager had ever observed a representative differing from the titration schedule detailed in the SPC. One commented that generally accepted best practice was to have the customer repeat back the titration schedule in order to ensure that they fully understood the process.

ProStrakan stated that there was no specific briefing document on the use of the Abstral Titration Chart. The Abstral initial training course covered the titration process in detail (copies of the relevant training slides were provided - Module Three: Abstral Product Profile and Clinical Value (ref M017/0456)). The titration process for Abstral was covered in detail on page seven of this slide deck and ProStrakan considered that this was fully consistent with the titration schedule detailed in the Abstral SPC.

ProStrakan also provided a copy of the Abstral Titration Wheel (ref M017/0527) which was a further aid to the appropriate and recommended use of Abstral. As with the titration chart it could be distributed to health professionals at meetings and was certified before use.

In conclusion, ProStrakan stated that its representatives were thoroughly trained on the Abstral titration schedule. Indeed, this was a key component of the recommended use of the product. This training informed the correct use of a selection of promotional materials that in themselves aided understanding of the titration process and supported health professionals in the appropriate use of Abstral. ProStrakan considered that the training materials met the requirements of the Code and thus denied a breach of Clause 15.9. ProStrakan also maintained that its representatives were well aware of these standards as demonstrated in the interviews conducted as part of its investigation into this complaint. ProStrakan denied a breach of Clause 15.2.

ProStrakan submitted that further to this, the materials produced in support of this assertion themselves complied with the Code with regards to accuracy and accordance with the marketing authorization for the product. The titration schedule detailed in the titration chart and the titration wheel reflected the Abstral SPC. ProStrakan did not consider that Clauses 3.2 or 7.2 had been breached.

ProStrakan stated that neither the interviews nor the material review identified claims that were not capable of substantiation. ProStrakan thus denied a breach of Clause 7.4.

ProStrakan considered that high standards had been upheld, and no breach of Clause 9.1 had occurred. As a consequence it also considered that a ruling of a breach of Clause 2 was not justified in this instance.

ProStrakan stated that without a formal identification of the material in question or any further detail about

the representative concerned, a full investigation into the complaint was not possible. Whilst ProStrakan respected the complainant's anonymity, it noted that an anonymous complaint limited the company's ability to investigate the allegations in detail and deprived the company of the standard reassurances provided to companies by the PMCPA that the complainant had been asked to declare any conflict of interest.

In response to a request for further information, ProStrakan submitted that without a name or location to work from it was difficult to exactly define the scope of the investigation. However, given that the complainant identified him/herself as a 'pain physician' and not a general practitioner, ProStrakan assumed that he/she worked in secondary care and so it focussed its interviews on the specialist care team (SCT) which was responsible for promoting Abstral in secondary care only.

ProStrakan stated that it would not have been possible to interview every member of the SCT before it submitted its response in the timeframe available, so it interviewed all of the regional business managers (RBMs) for the team and one of the two representatives in the SCT who covered Scotland; the other representative had only just been appointed when the complaint was made. The individual interviewed did not recognise the titration schedule detailed by the complainant and did not know of anywhere in Scotland that used such a system. This view was also reflected by the RBM who covered the North of England and Scotland.

ProStrakan submitted that in addition to the field force interviews, head office staff, including senior managers involved in the commercialisation of Abstral, were also involved in the investigation. Details of those interviewed were provided.

ProStrakan stated that palliative care physicians were a key customer group for Abstral, and so its representatives regularly worked with them to educate prescribers on the appropriate use and titration of the product. In 2008, when Abstral was launched in the UK, materials were developed in collaboration with a leading palliative care physician. These items had subsequently expired and been discontinued. More recent materials had been developed in collaboration with palliative care physicians, but these materials did not match the description provided by the complainant and did not explicitly relate to titration.

As a part of its commitment to the support of UK healthcare and healthcare providers, ProStrakan offered financial support through sponsorship, grants and donations to those who requested such. This support was offered in accordance with the Code and approved in accordance with ProStrakan's relevant standard operating procedure (SOP). Sponsorship, grant and donation records were checked for the last two years. ProStrakan's records showed that a proportion of this funding had been provided to palliative care teams. However, this funding had almost exclusively supported attendance at educational events. The records did not show a funding request for a project which had resulted in a document such as that described by the complainant. One funding request directly related to the titration of Abstral and had been submitted by a physician seeking financial support to design and print a titration tool to assist health professionals in using Abstral. The financial support for this project had been approved but the item was still in development and had not yet been released.

ProStrakan stated that it was not currently part of any joint working agreements with anyone working in palliative care.

PANEL RULING

The Panel noted that the anonymous complainant had not provided any details as to where he/she worked; no details were provided as to the identity of the representative alleged to have given the complainant misinformation. The complainant had referred to being shown a document which had been developed by a palliative care team in Scotland; the complainant had not been given a copy and no documents were provided by the complainant in support of his/her complaint. The complainant was non-contactable and thus it was not possible to request further information. The Panel noted that, 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 from the SPC, that Abstral was indicated for the management of breakthrough cancer pain (BTcP) in adults using opioids for chronic cancer pain. All patients must start Abstral therapy with a single 100mcg sublingual tablet. If adequate analgesia was not obtained in 15-30 minutes a second 100mcg tablet could be given. If adequate analgesia was not obtained within 15-30 minutes of the first dose, an increase in dose to the next highest tablet strength should be considered for the next episode of BTcP. Dose escalation should continue in a stepwise manner until adequate analgesia was achieved. The dose strength for the supplemental (second) sublingual tablet should be increased from 100 to 200mcg at doses of 400mcg and higher. The maximum dose for the treatment of any episode of BTcP was 800mcg.

The Panel noted that ProStrakan had provided a copy of the Abstral Titration Chart which it assumed was the document referred to by the complainant although it had not been developed in collaboration with a Scottish palliative care team. This chart showed that for the first episode of BTcP, patients should be given a 100mcg tablet with the option of a second tablet if the first was not effective after 15-30 minutes. If a second tablet had to be given then treatment of the second episode of BTcP should begin with a 200mcg tablet with an option of an additional 100mcg tablet if the 200mcg tablet did not provide adequate analgesia within 15-30 minutes. Treatment of the third episode of BTcP should begin with a 300mcg tablet and the titration schedule

continued in this stepwise manner until adequate analgesia or the maximum dose (800mcg) was achieved, whichever came sooner. The Panel noted the layout of the titration chart and queried whether the complainant had mistaken BTcP episodes 1 to 6 with treatment days 1 to 6. In the Panel's view the titration chart was in accordance with the titration schedule contained within the Abstral SPC.

The Panel noted that in training slides 'Abstral:product profile and clinical value' a slide headed 'Titration of Abstral' correctly referred to doses being increased, if necessary, with subsequent episodes of BTcP. Similarly the titration wheel showed that if a rescue dose had been required then the dose of the first tablet should be increased for the next episode of pain.

The Panel noted that ProStrakan had not been able to find evidence that any of its staff knew anything about the daily titration schedule referred to by the complainant. All of the materials provided by ProStrakan referred to the dose of Abstral being increased, if necessary, with subsequent episodes of BTcP in accordance with the SPC. On the basis of the information before it, the Panel considered that the complainant had not established, on the balance of probabilities, that a representative had advised him/her to titrate Abstral on a daily basis as alleged. No breach of Clauses 2, 3.2, 7.2, 7.4, 9.1 15.2 and 15.9 was ruled.

Complaint received **7 June 2012**

Case completed **2 July 2012**

ANONYMOUS EMPLOYEE v GRÜNENTHAL

Promotional mailings

An employee of Grünenthal complained anonymously about the frequency and volume of Palexia (tapentadol) promotional mailings sent to health professionals and alleged that target customers would be sent a mailing after every call. The complainant noted that the Code stated that 'Restraint must be exercised on the frequency of distribution and on the volume of promotional material distributed' and that 'No more than eight mailings for a particular medicine may be sent to a health professional in a year'. The complainant alleged that as Palexia mailings were sent to target customers after every call, in addition to other Palexia mailings, some customers could get more than eight mailings in a year and/or several mailings in a short space of time.

The detailed response from Grünenthal is given below.

The Panel noted that the supplementary information referred to by the complainant stated, *et al*, that in the first six months following the launch of a new medicine, a health professional could be sent up to four mailings about the medicine and that no more than eight mailings for a particular medicine might be sent to a health professional in a year.

The Panel noted that a marketing newsletter provided by the complainant implied that a Palexia brand reminder mailing would be sent to target GPs after every call. Grünenthal submitted that this was not so; the mailing would only be sent once, following the first contact with the customer in relation to Palexia from April 2012. This point could have been more clearly stated in the newsletter.

With regard to the volume of mailings the Panel noted that Grünenthal had provided information to show that between February 2011 and June 2012 no GP would have received more than four Palexia mailings and the maximum number received by any hospital health professional was two. The Panel considered that there was no evidence to show that any health professional had received more than eight mailings in a year as alleged. No breach of the Code was ruled.

With regard to the frequency of mailings the Panel noted that it was possible that some GPs might have received the MIMS Palexia announcement mailing (sent March 2012), the brand reminder mailing (sent from April 2012) and two mailings about a meeting (sent May-June 2012) in successive months. The Panel considered that in the circumstances this was not unacceptable. No breach of the Code was ruled.

The Panel consequently considered that with regard to the requirements for mailings there had not been a failure to maintain high standards. No breach of the Code was ruled.

An anonymous, non-contactable employee of Grünenthal Ltd complained about the frequency and volume of Palexia (tapentadol) promotional mailings sent to health professionals.

COMPLAINT

The complainant alleged that after every call made on a target customer, Grünenthal sent that customer a Palexia 'brand reminder mailer' and dosage card. The complainant noted that Clause 11.2 of the Code stated that 'Restraint must be exercised on the frequency of distribution and on the volume of promotional material distributed' and also that 'No more than eight mailings for a particular medicine may be sent to a health professional in a year'. As mailings were sent after every call made on target customers, in addition to other promotional mailings for Palexia, some customers could get more than eight mailings in a year and/or several mailings in a short space of time.

The complainant provided a copy of a marketing newsletter which was sent to representatives in March. The newsletter stated that the brand reminder mailing would enhance the memorability of representatives' calls. The reader was informed that 'Your call on any IPTI customer with Palexia will be picked up in [the customer relationship management system], and then within 7 days we will mail the customer a letter and an additional dosage card reminding them of the call you made. This will start from the end of March.' The newsletter also referred to a second mailing programme which would also start in March, ie the MIMS product announcement on Palexia which would go to 10,000 UK specialists.

When writing to Grünenthal, the Authority asked it to respond in relation to Clauses 9.1 and 11.2 of the Code.

RESPONSE

Grünenthal explained that the Palexia brand reminder mailing (ref P12 0056a), referred to by the complainant was designed as a contact-activated mailer to selected GPs (maximum 4,500). The mailing consisted of a letter which reviewed the content of that contact and a dosage and titration leavepiece (ref P12 0056). The mailings were first sent out in April 2012 and this initiative would continue until December 2012. The process behind the mailing was automatic to ensure that it was only sent once to any GP during its eight month active period.

Grünenthal explained that the representative entered their activity into the company's customer relationship management system on a weekly basis. At the end of each week the software generated a list of those health professionals who had been seen for the first time since April 2012 with Palexia.

This list was sent to a mailing provider and it checked the list against previous 2012 recipients of the mailing to ensure no duplication could occur. Once the list was finalised, the mailing was posted with the dosage card to the health professional. To date, since April 2012, the mailing had been sent to nearly 500 GPs. The overall list of those who had received the mailing since April 2012 was stored at the mailing provider and was available to Grünenthal's marketing team.

Grünenthal submitted that for planning purposes the brand reminder mailing counted as one promotional mailing contact per health professional for Palexia, to the company's selected group of GPs. Grünenthal further explained that the MIMS product announcement mailing (ref P12 0029) was a one-off mailing sent in March 2012 to 11,000 GPs. The list was mailed by MIMS and Grünenthal's marketing team had access to the full list of recipients. Again, for planning purposes this mailing counted as one promotional mailing contact per health professional for Palexia to a selected group of GPs.

Grünenthal submitted that, overall, its brand planning process determined and clarified the intended activity regarding promotional posted mailings over the calendar year for each product in line with the requirements of the Code. This process for any year was usually completed and agreed during October of the previous year, and the review process ensured that the volume and frequency of planned mailings was regulated and appropriate. It also ensured that a health professional did not receive several mailings in a short period of time. There were planned promotional mailings for Palexia throughout 2012. The list of intended audiences for those mailings was maintained in a smartsheet excel planner, which gave a clear overview of the maximum number of promotional mailings that any health professional could receive from Grünenthal about Palexia.

Grünenthal provided information of promotional mailings for Palexia that had been sent to health professionals since February 2011. In addition to the brand reminder mailing (from April – December 2012) and the MIMS product announcement mailing (March 2012), GPs in two English counties received a mailing about a meeting (May/June 2012) (which had to be re-sent to one group due to a date change (June 2012)). With regard to secondary care, Grünenthal had invited some key opinion leaders to a round table meeting (September 2011) and 200 health professionals to a meeting in London (May 2012). Five hundred secondary care health professionals in Scotland had been sent a Palexia SMC (Scottish Medicines Consortium) mailing (May 2012). Grünenthal submitted that from February 2011 to June 2012, and allowing for the on-going nature of the contact-activated mailings, and the geographies used for other mailings, the maximum number of Palexia promotional mailers that any single GP could have received in that time was four and any single secondary care health professional was two.

Grünenthal concluded that it had demonstrated that it operated within the Code regarding the frequency and volume of promotional mailings and it thus denied a breach of Clause 11.2. Grünenthal considered that it had maintained high standards at all times and it thus denied a breach of Clause 9.1.

PANEL RULING

The Panel noted that Clause 11.2 of the Code stated that restraint must be exercised on the frequency of distribution and on the volume of promotional material distributed. Supplementary information to the clause stated, *et al*, that in the first six months following the launch of a new medicine, a health professional could be sent up to four mailings about the medicine and went on to state that no more than eight mailings for a particular medicine might be sent to a health professional in a year.

The Panel noted that the marketing newsletter provided by the complainant implied that a Palexia brand reminder mailing would be sent to target GPs after every call. Grünenthal submitted that this was not so; the mailing would only be sent once, following the first contact with the customer in relation to Palexia from April 2012. This point could have been more clearly stated in the newsletter.

With regard to the volume of mailings the Panel noted that Grünenthal had provided information to show that between February 2011 and June 2012 no GP would have received more than four Palexia mailings and the maximum number received by any hospital health professional was two. The Panel considered that there was no evidence to show that any health professional had received more than eight mailings in a year as alleged. No breach of Clause 11.2 was ruled.

With regard to the frequency of mailings the Panel noted that it was possible that some GPs in one English county who had met a Grünenthal representative and discussed Palexia might have received the MIMS Palexia announcement mailing (sent March 2012), the brand reminder mailing (sent from April 2012) and two mailings about a meeting (sent May-June 2012 – the second mailing was sent due to a date change) in successive months. The Panel considered that in the circumstances this was not unacceptale. No breach of Clause 11.2 was ruled.

The Panel consequently considered that with regard to the requirements for mailings there had not been a failure to maintain high standards. No breach of Clause 9.1 was ruled.

Complaint received **13 June 2012**

Case completed **26 June 2012**

CODE OF PRACTICE REVIEW – August 2012

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

2475/1/12	**Pfizer v Johnson & Johnson**	**Nicorette Invisi Patch leavepiece**	**Two breaches Clauses 7.2, 7.3 and 7.4** **Breach Clause 7.8** **Two breaches Clauses 7.9 and 7.10** **Breach Clause 8.1** **Two breaches Clause 9.1**	**Appeal by respondent**	**Page 3**
2479/2/12 and 2480/2/12	Novo Nordisk v Bristol-Myers Squibb and AstraZeneca	Arrangements for a symposium	No breach	No appeal	Page 14
2481/2/12	**Muslim Affairs Specialist v ProStrakan**	**Promotion of Adcal-D_3 Caplets**	**Breaches Clauses 7.2, 7.4, 9.1 and 15.9**	**Appeal by respondent**	**Page 20**
2482/2/12	**Anonymous v Novo Nordisk**	**Invitation to a meeting**	**Breach Clause 9.9**	**Appeal by complainant**	**Page 26**
2488/3/12	**Lead Pharmacist v Meda**	**Email promotion of EpiPen**	**Breaches Clauses 9.9 and 12.1**	**Appeal by respondent**	**Page 32**
2490/3/12	**Voluntary admission by Bayer Healthcare**	**Conduct of an employee**	**Breaches Clauses 2, 3.1, 4.1, 4.10 and 4.11** **Twenty breaches Clause 7.2** **Breach Clause 7.3** **Eight breaches Clause 7.4** **Breaches Clauses 9.1, 12.1, 14.1 and 15.2**	**No appeal**	**Page 37**
2492/3/12	**Prescribing Advisor v Meda**	**EpiPen Booklet**	**Four breaches Clauses 7.2** **Two breaches Clause 7.4** **Breach Clause 9.1**	**No appeal**	**Page 45**
2493/3/12	**General Practitioner v AstraZeneca**	**Invitation to an advisory board**	**Breach Clause 20.1**	**No appeal**	**Page 48**
2494/3/12	Norgine v Galen	Trustsaver campaign	No breach	No appeal	Page 54

2495/3/12	Pharmacist v ALK-Abelló	Alleged conduct of a representative	No breach	No appeal	Page 63
2497/4/12	Pharmacosmos v Vifor	Competitor dosing information	No breach	No appeal	Page 66
2498/4/12	**Sandoz v Merck Serono**	**Patient support item**	**Breach Clause 18.2**	**No appeal**	**Page 69**
2499/4/12	**Pharmacist Adviser v Sanofi**	**Mozobil email**	**Breaches Clauses 7.2 and 15.2**	**No appeal**	**Page 71**
2500/4/12	**Anonymous v Eisai**	**Promotion of Zonegran**	**Breaches Clauses 7.2, 7.10 and 9.1**	**No appeal**	**Page 74**
2503/5/12	**General Practitioner v Genus**	**Promotion of Cetraben**	**Breach Clause 9.2**	**No appeal**	**Page 78**
2505/5/12	Anonymous v ProStrakan	Promotion of Abstral	No breach	No appeal	Page 81
2510/6/12	Anonymous v ProStrakan	Promotion of Abstral	No breach	No appeal	Page 86
2513/6/12	Anonymous Employee v Grünenthal	Promotional mailings	No breach	No appeal	Page 90

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 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 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 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 is neither present nor participates 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 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, are always 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.

Complaints under the Code should be sent to the Director of the Prescription Medicines Code of Practice Authority, 7th Floor, Southside, 105 Victoria Street, London SW1E 6QT

telephone 020 7747 8880
facsimile 020 7747 8881
by email to: complaints@pmcpa.org.uk.