NUMBER 70 NOVEMBER 2010

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.

2011 CODE NOW AVAILABLE

The ABPI Code of Practice for the Pharmaceutical Industry 2011 is now available to download from the PMCPA website. The proposals to amend the Code were agreed by the ABPI on 2 November 2010.

The 2011 Code will come into effect on 1 January 2011 but with a transitional period before becoming fully operative on 1 May 2011. During the period 1 January 2011 to 30 April 2011, 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.

There are longer transitional provisions for Clauses 20.2, 20.3 (public disclosure of payments to consultants), Clause 19 (public disclosure of sponsorship of attendance at meetings organised by third parties) and Clause 18.6 (public disclosure of medical and educational goods and services in the form of donations and grants). Details are given in the supplementary information to those clauses.

As well as the 2011 Code itself, the changes agreed at the ABPI meeting, a set of slides detailing the main changes to the Code and a summary of responses to the consultation are available from the PMCPA website. Printed copies of the 2011 Code will be available before the end of the year and can be ordered by emailing Lisa Matthews at lmatthews@pmcpa.org.uk.

Principal changes

Changes have been made to Clauses 1, 3, 4, 5, 7, 9, 12, 13, 14, 15, 16, 18, 19, 20, 22 and 23 in the 2011 Code. Not all changes are detailed below. Please ensure you read the changes to the Code and other supporting documents available from the PMCPA website.

General updating
Redundant transitional arrangements for Clauses 4, 5 and 13 have been removed. As branded promotional aids for health professionals are no longer permitted, Clauses 3, 4, 5, 15 and 19 have been amended.

Clause 1
A definition of 'promotional aid' has been added and additional information regarding examples of promotion included in the supplementary information.

Clause 5
Additional clarity has been provided regarding the content of abbreviated advertisements.

Clause 7
Additional supplementary information has been provided regarding absolute and relative risk.

Clause 9
New supplementary information has been added which requires promotional emails to contain information of how to unsubscribe. Clarification has also been provided about responding to enquiries by email.

A new requirement for pharmaceutical companies to clearly declare involvement in sponsored material relating to human health or diseases has been added. The supplementary information also provides more

continued overleaf

PUBLIC REPRIMANDS FOR NOVO NORDISK

Novo Nordisk Limited has been publicly reprimanded by the Code of Practice Appeal Board in relation to two matters. Firstly for promoting liraglutide prior to the grant of its marketing authorization (Case AUTH/2234/5/09) and secondly for the provision of inaccurate information to the Code of Practice Panel (Case AUTH/2269/9/09).

The Appeal Board was extremely concerned about Case AUTH/2234/5/09; the promotion of a medicine prior to the grant of its marketing authorization was a serious matter and displayed a poor understanding of the requirements of the Code. The Appeal Board was not convinced that Novo Nordisk fully understood the seriousness of the matter and was especially concerned to note that in another case recently the company had similarly been found in breach of the Code for promoting liraglutide prior to the grant of its marketing authorization (Case AUTH/2202/1/09).

In Case AUTH/2269/9/09 the Appeal Board considered that the provision of inaccurate information, the delayed withdrawal of a supplement (at issue in Case AUTH/2202/1/09) and its continued availability on Novo Nordisk's website despite the efforts to withdraw it demonstrated poor management practices. The undertaking in Case AUTH/2202/1/09 had been signed based on inaccurate information provided by a senior manager. In the Appeal Board's view there appeared to be no inherent sense of personal responsibility for compliance with the Code or a full understanding of what that meant. The Appeal Board considered that responsibility for the company culture in that regard resided with the senior management and was apparently lacking. The Appeal Board also expressed concern about the apparent lack of leadership from the medical department.

In Case AUTH/2234/5/09 and Case AUTH/2269/9/09 the Appeal Board required an audit and subsequent re audits of Novo Nordisk's procedures.

Full details of Case AUTH/2234/5/09 can be found at page 3 of this issue of the Review and the report for Case AUTH/2269/9/09 appears at page 25.

CODE OF PRACTICE TRAINING

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

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

The next Code of Practice seminar dates on which places remain available are:
Monday, 24 January 2011
Monday, 28 February 2011

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
12 Whitehall, London SW1A 2DY

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

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.

ABPI CODE OF PRACTICE Continued

guidance regarding the wording of such declarations.

Clause 13
A new requirement to publish summary details and results of non-interventional studies has been added.

Clause 14
The role of pharmacists has been expanded to allow them to certify promotional material instead of medical practitioners. Additional certification requirements have been added in relation to joint working and patient support programmes.

Clause 16
Clarification of time periods to take the ABPI examinations and further information about when extensions can be agreed have been included.

Clause 18
There have been a lot of changes to this clause. Some of the principal changes are:

- the provision of branded promotional aids to health professionals is no longer permitted
- patient support items may be made available
- quizzes cannot be conducted from exhibition stands
- text books cannot to be given as promotional aids
- medical and educational goods and services cannot be provided to individuals for their personal benefit
- new requirements regarding joint working
- donations and grants to certain institutions and organisations made from 2012 must be made public.

Clause 19
Sponsorship for health professionals and appropriate adminstrative staff to attend meetings organised by third parties in 2012 and in each year thereafter must be publicly disclosed.

Declarations must include the total amount paid in a calendar year, the total number of recipients and the total number of attendances sponsored.

Clause 20
There are new requirements for companies to contract consultants to declare their arrangements with a company when they write or speak in public about the matter.

The total amount of fees paid to consultants and the total number of consultants for certain services used in 2012 and in each year thereafter will need to be publicly disclosed. This applies to all health professionals and appropriate administrative staff when used as consultants in the UK.

Clause 23
Monetary support and/or significant indirect/non financial support of patient organisations with a value of £250 or more per project which commenced on or after 1 May 2011 or was ongoing on that date will need to be publicly disclosed.

CASE AUTH/2234/5/09

LILLY v NOVO NORDISK

Promotion of Victoza prior to the grant of its marketing authorization

Lilly alleged that, despite being recently ruled in breach of the Code for promoting Victoza (liraglutide) prior to the grant of a marketing authorization (Case AUTH/2202/1/09), Novo Nordisk continued to so promote Victoza. Lilly's product Byetta (exenatide) was licensed for the treatment of type 2 diabetes mellitus in combination with metformin and/or sulphonylureas in patients who had not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.

Novo Nordisk advised that Victoza had been granted a marketing authorization on 30 June 2009.

The detailed response from Novo Nordisk is given below.

Lilly alleged that an online educational resource sponsored by Novo Nordisk involved the pre-licence discussion and promotion of liraglutide. Lilly noted that a screen which it accessed in April 2009 stated 'Thank you for registering with Liraglutide online!' and appeared when the 'New User Registration' hyperlink was activated.

In inter-company correspondence, Novo Nordisk stated that this was an 'oversight' and that 'measures will be implemented as soon as possible', instead of immediately, to address this. Lilly refuted the suggestion that this was an unintentional error; 'Thank you for registering with Liraglutide online!' clearly demonstrated Novo Nordisk's intent to use the training module for pre-licence promotion of liraglutide. The removal of this wording did not negate Lilly's allegation.

Lilly cited a number of examples throughout the online resource in support of its allegations that promoted liraglutide prior to the grant of its marketing authorization and misleadingly compared liraglutide with its product Byetta which, unlike liraglutide, was licensed. Lilly further alleged that some of the comparisons had disparaged Byetta. Lilly's detailed allegations are given below. Lilly further noted that it was only at the end of Section 4.2.1 titled 'Overview' that the statement 'Liraglutide is not yet licensed in the UK' appeared in very small font such that it was almost obscured. Lilly alleged that this did not however mitigate the substantive issue in question.

Lilly also noted that the availability of this website was highlighted in the 'Resources and Support' section of Prescriber, 5 March 2009. Lilly alleged that promoting the availability of the website to the medical press effectively also supported the pre-licence promotion of liraglutide.

Lilly alleged that this activity constituted the pre-licence promotion of liraglutide, it invited misleading claims and comparisons with licensed medicines and represented the disguised promotion of liraglutide. Lilly alleged breaches of the Code including a breach of Clause 2.

The Panel was extremely concerned to see that following registration a message 'Thank you for registering with Liraglutide online!' appeared. This was compounded by the name of the website 'Realising the promise of the GLP-1 receptor.' The Panel considered that the first impression was not of an educational online resource but promotion of liraglutide as alleged. The Panel noted that Novo Nordisk had removed the reference to liraglutide.

Overall the Panel was extremely concerned about the material in question. It included detailed information about liraglutide, a product that did not have a marketing authorization. The Panel considered that the material promoted liraglutide. In this regard the Panel noted the initial references to exenatide and the failure to be very clear about the differences in the regulatory status of the products. A breach of the Code was ruled. The material was misleading and included misleading comparisons. Breaches of the Code were ruled. The Panel ruled a breach of the Code in relation to a section on tolerability and safety. The Panel did not consider the material disparaged Byetta and no breach of the Code was ruled. The material was disguised promotion and a breach of the Code was ruled. High standards had not been maintained and a breach of the Code was ruled.

The Panel noted that promoting a medicine prior to the grant of the marketing authorization was an activity likely to be in breach of Clause 2. That clause was used as a sign of the particular censure. The Panel ruled a breach of Clause 2.

The front cover of the Sponsored supplement in The British Journal of Diabetes & Vascular Disease, November/December 2008, Volume 8 Supplement 2, 'The Modulating Effects of GLP-1 in Type 2 Diabetes: Proceedings from a symposium of the 43rd Annual Meeting of the European Association for the Study of Diabetes [EASD] Amsterdam, The Netherlands, 17 September 2007' stated 'This supplement has been supported by an educational grant from Novo Nordisk'. Lilly alleged that the supplement was being used promotionally by Novo Nordisk as evidenced by its distribution in the UK with The British Journal of Diabetes & Vascular Disease, January/February 2009, Volume 9 Issue 1.

Lilly alleged that the title and reference to the

EASD Annual Meeting misleadingly implied that the supplement was independent. This was further compounded by the format and layout of the supplement which suggested it was a part of and integral to the accompanying medical journal. The statement 'This supplement has been supported by an educational grant from Novo Nordisk' on the cover disguised the promotional nature of the material, which was in fact a paid for insert, editorially controlled by Novo Nordisk, detailing the proceedings of the company's sponsored satellite symposium which involved the pre-licence promotion of liraglutide.

The author, and chair of the satellite symposium introduced the five articles and stated 'Agents such as the GLP-1 receptor agonist exenatide and the DPP-4 inhibitors sitagliptin and vildagliptin are now available (the latter not in the USA) for utilisation in regimens to treat type 2 diabetes, while the GLP analogue liraglutide may soon be available'. Lilly alleged that the unlicensed status of liraglutide was not clearly stated and that its availability was underplayed relative to the wording adopted for vildagliptin. Lilly noted that it was only here that the derivation of four of the five articles was explained, albeit briefly, and linked to '… a symposium held on 17 September 2007, during the European Association for the study of Diabetes Meeting in Amsterdam'; although Novo Nordisk's sponsorship was omitted.

Lilly cited a number of examples with regard to the alleged promotion of liraglutide prior to the grant of its marketing authorization.

Lilly also alleged that a common theme in this insert was to misleadingly associate the discussion of liraglutide alongside licensed treatments such as Byetta thus creating the misleading impression that liraglutide should be regarded in the same context as Byetta, a licensed treatment.

Lilly noted liraglutide's unlicensed status and alleged that a discussion about its long-term effects on progression of type 2 diabetes (remarkable for a medicine that was not yet licensed!), clearly invited the suggestion that liraglutide was clinically relevant in the treatment of type 2 diabetes and available. This impression was reinforced in a 'Key messages' box which reiterated the messages that 'Liraglutide is a once-daily GLP-1 analogue that has a promising clinical profile including substantial improvement in glycaemic control without a risk for hypoglycaemia, and weight loss as an added benefit'.

Lilly alleged that an article 'Mechanisms behind GLP-1 induced weight loss' invited a discussion of liraglutide data and its effect on weight loss, and by reference to licensed medicines such as exenatide and sitagliptin invited the reader to consider it as 'a desirable option for the treatment of type 2 diabetes, as [it] improves[s] glycaemic control, improve[s] pancreatic function and induce[s] clinically meaningful weight loss' and its '…potential to modify type 2 diabetes disease progression'.

Lilly noted that although this article was not from the Novo Nordisk satellite symposium it involved editorial input from a Novo Nordisk employee as evidenced by the 'Acknowledgements' which stated 'The author has received many helpful comments to the manuscript from [a named doctor] ...'; this being a senior specialist from Novo Nordisk.

In conclusion, Lilly alleged that presenting the output of a Novo Nordisk run meeting as an independent supplement to a journal demonstrated poor knowledge of the Code. Health professionals generally looked to medical journals as a source of independent information therefore Novo Nordisk should have made it clear that the authors wrote the articles on behalf of and as a result of its promotional activities. Lilly alleged that the misleading description and presentation of this insert and its pre-licence promotion of liraglutide represented a breach of the Code.

Lilly alleged that this activity constituted the pre-licence promotion of liraglutide, it invited misleading claims and comparisons with licensed medicines and represented the disguised promotion of liraglutide in breach of the Code including Clause 2.

The Panel noted that the supplement had been initiated by Novo Nordisk and its agency. The authors were mostly those who had taken part in the company sponsored symposium.

The Panel considered that Novo Nordisk was inextricably linked to the production of the supplement. There was no arm's length arrangement between the provision of the sponsorship and the generation of the supplement. Circulation was not limited to those who attended the Novo Nordisk sponsored meeting as it was circulated with The British Journal of Diabetes and Vascular Disease in the UK. The Panel noted that it was an established principle under the Code that UK companies were responsible for the activities of overseas affiliates that came within the scope of the Code. Thus Novo Nordisk UK was responsible under the Code for the distribution in the UK.

Given the company's involvement and the content of the supplement, the Panel considered that the supplement was, in effect, promotional material for liraglutide. The Panel considered that the material was a paid-for insert from Novo Nordisk, not a supplement from The British Journal of Diabetes and Vascular Disease for which the journal's editorial board would have been responsible. The insert was distributed with The British Journal of Diabetes and Vascular Disease when liraglutide did not have a UK marketing authorization. The Panel considered that the insert promoted liraglutide to UK health professionals prior to the grant of its marketing authorization. A breach of the Code was ruled.

The insert misleadingly implied that liraglutide was licensed which was not so. A breach of the Code was ruled. The insert also invited the reader to make misleading comparisons about the licensed status of GLP-1-based therapies as alleged. A breach of the Code was ruled. The insert implied that it was a report of an independent meeting. The Panel considered that the insert was disguised promotion and a breach of the Code was ruled. The Panel considered that the role of Novo Nordisk was not clear. It was misleading to merely state that the insert had been supported by an educational grant from Novo Nordisk when the meeting was a Novo Nordisk sponsored symposium. The Panel considered that high standards had not been maintained and a breach of the Code was ruled.

The Panel considered that presenting the output of a Novo Nordisk meeting as an independent supplement to a journal demonstrated apparent poor knowledge of the Code. Health professionals generally looked to medical journals as a source of independent information; where authors wrote on behalf of pharmaceutical companies this must be clear. In the Panel's view the majority of readers would have viewed the material at issue quite differently if they had known that it was the report of a company sponsored meeting. The Panel considered that the description and presentation of the insert was such as to reduce confidence in, and bring discredit upon the pharmaceutical industry. A breach of Clause 2 was ruled.

Lilly stated that a promotional Symposium on Diabetes Care, March 2009, sponsored by Novo Nordisk, concluded with a 'Key Note Lecture' which was chaired by a senior clinical nurse specialist and included a one hour lecture/presentation 'A New Molecule in Diabetes – From Conception to Reality' delivered by a senior specialist, Novo Nordisk.

Lilly alleged that from this presentation it appeared that Novo Nordisk had intentionally commercialised liraglutide by a keynote lecture to promote the product and misleadingly imply that it was a licensed and relevant treatment option for the management of diabetes. This was evidenced by the context in which this particular lecture was presented ie preceded by an extensive discussion of subjects such as 'Diabetes – A Weighty Issue, New Treatments, Guidelines for Diabetes Care'.

Lilly alleged that this activity again constituted the pre-licence promotion of liraglutide, it invited misleading claims and comparisons with licensed medicines and represented the disguised promotion of liraglutide in breach of the Code including Clause 2.

The Panel noted that Novo Nordisk was responsible for the meeting. The title of the final presentation 'A New Molecule in Diabetes – From Conception to Reality' implied that the new molecule (liraglutide) was available for use which was not so. No details had been provided about the delegates. The Panel noted that the content referred to GLP-1 and its clinical potential as well as GLP-1 analogues. It included detailed information about liraglutide. The presentation compared liraglutide with exenatide, vildagliptin, glimepiride, rosiglitazone and glargine. The last few slides compared liraglutide and exenatide in relation to HbA_{1c}, HOMA, body weight and frequency of nausea. Each parameter favoured liraglutide and the HbA_{1c} and HOMA data were statistically significant. The final slide showed advantages for exenatide compared with glargine in relation to a composite endpoint of $HbA_{1c} \leq 7.4\%$ and weight gain $\leq$ 1kg. There did not appear to be any mention of the licensed status of the product. The final slide concluded that GLP-1 based therapies were highly interesting for treatment for type 2 diabetes and that GLP analogues might be made once daily treatments.

The Panel considered that the presentation promoted liraglutide when it did not have a marketing authorization. Thus the Panel ruled a breach of the Code as alleged. The title of the presentation was misleading and a breach of the Code was ruled. The presentation included comparisons with licensed medicines and could be seen as taking unfair advantage of the reputation of licensed medicines; thus a breach of the Code was ruled. The Panel did not consider that the meeting constituted the disguised promotion of liraglutide. The presentation was clearly promotional and no breach of the Code was ruled.

The Panel considered that high standards had not been maintained and ruled a breach of the Code. The Panel noted that promoting a medicine prior to the grant of the marketing authorization was an activity likely to be in breach of Clause 2. That clause was used as a sign of particular censure. The Panel ruled a breach of Clause 2.

Lilly noted that Novo Nordisk, together with an endocrine and diabetes society, was developing a local research strategy involving collaboration between centres in that area. To support this, a senior member of Novo Nordisk's sales department helped convene/facilitate the meeting, February 2009 which included discussion of liraglutide data in diabetes and obesity, the latest Levemir (insulin detemir) data, ongoing development/research projects and opportunities for collaboration in areas of pharmacological research in the local area amongst other things. Novo Nordisk extended an open invitation for any health professionals interested in participating in collaborative research projects to attend.

Lilly alleged that this was clearly a promotional meeting sponsored by Novo Nordisk as evidenced by the tacit and direct involvement of sales and marketing staff; this was acknowledged by Novo Nordisk in inter-company correspondence. Lilly queried why a member of the sales department would be involved in a meeting purporting to be focused on the information needs of 'potential and existing investigators' and where the objective was

'to update [delegates] on current and future research projects'.

Lilly alleged that the discussion of liraglutide data and other medicine development/research projects and data constituted pre-licence disguised promotion of liraglutide in breach of the Code including Clause 2.

The Panel noted that few details had been provided about this meeting. A presentation about 'On going development projects' had been given. The meeting appeared to have been held in response to an unsolicited request from the society for an update on ongoing and future research projects. From the agenda all of the speakers were from Novo Nordisk. The Panel was concerned that a senior member of the company's sales department had attended, albeit by invitation. The impression that that gave was important.

The Panel examined the slides used by Novo Nordisk for the presentation 'On going development projects'. The introduction referred to insulin research and development including future insulins and products Novo Nordisk was working on. It also referred to GLP-1 development. Information was presented about a study on islet transplantation which ran from April 2009.

The Panel was concerned that based on Novo Nordisk's activities already considered above, it was possible that liraglutide had been promoted to the audience. The Panel considered that this meeting appeared to be different to the one at issue above in that it was organised by Novo Nordisk in response to a request that the meeting be held. However the complainant had the burden of proving their complaint on the balance of probabilities. The Panel considered that given all the circumstances and the limited evidence before the Panel, the meeting could be regarded as the legitimate exchange of scientific information. Delegates were invited as potential or existing investigators, not as prescribers per se. No breach of the Code was ruled including Clause 2.

Lilly alleged that a promotional diabetes network meeting in March 2009 sponsored by Novo Nordisk invited presentations and discussions about the management of type 2 diabetes and presented information and various data about liraglutide, which, at the time, was unlicensed in the UK. A significant part of the meeting was devoted to a debate 'This house believes that GLP-1 agonists (such as exenatide and liraglutide) are the best second line therapy for type 2 diabetes'. Lilly alleged that the debate involved the presentation of liraglutide data to health professionals and engaged the audience in the pre-licence discussion of liraglutide and its place in the management of type 2 diabetes alongside licensed GLP-1-based therapies such as Byetta; this misleadingly implied that liraglutide was a licensed and relevant treatment option for the management of diabetes. The meeting was attended by Novo Nordisk sales representatives, which further exemplified the promotional nature of this meeting.

Lilly alleged that reference to topics on new treatment options in diabetes, the incretin system, modulators or mimetics of GLP-1, GLP-1 receptor agonists and the dipeptidyl IV receptor antagonists, stimulated a discussion on the availability of new treatments such as liraglutide thereby promoting the medicine prior to the grant of the marketing authorization. Lilly queried Novo Nordisk's assertion that only its regional medical advisor remained during the debate; this was contrary to the observations of Lilly staff who also attended.

Lilly alleged that this activity constituted the pre-licence promotion of liraglutide, it invited misleading claims and comparisons with licensed medicines and constituted the disguised promotion of liraglutide. As such it was in breach of the Code including Clause 2.

The Panel was concerned about the arrangements for the meeting. Novo Nordisk knew about the agenda about a month before the meeting. The topic of the debate that agents such as exenatide and liraglutide were the best second line therapy for type 2 diabetes was of concern given that one product had a marketing authorization and the other did not but was about to be so authorized. The title of the debate implied that both products were licensed which was not so.

The Panel noted that Novo Nordisk had denied the allegation that its sales representatives were present during the debate; Novo Nordisk submitted that only its local regional medical advisor was present. The Panel was concerned, given the title of the debate, that the regional medical advisor had attended even though Novo Nordisk submitted it had a clear lack of involvement in the debate. The Panel had similar concerns to those mentioned above. Novo Nordisk stated that the speakers were ultimately chosen by the main organiser of the meeting. There was no evidence before the Panel about the extent to which, if at all, Novo Nordisk had been able to influence or comment upon speaker selection. However Novo Nordisk had no involvement in the slide selection or topics for discussion. The Panel did not consider that Novo Nordisk's payment for an exhibition stand at the meeting meant that Novo Nordisk had sponsored the meeting and was responsible for its content. The Panel noted its concerns about the title of the debate and Novo Nordisk's knowledge thereof. However, on the evidence before it, the Panel decided that Novo Nordisk was not responsible for content of this meeting and thus no breaches of the Code were ruled including Clause 2.

The annual conference of a diabetes managed clinical network conference, April 2009 discussed various diabetes related topics by way of formal presentations and workshops and included a workshop focussing on the incretin mimetics. Lilly alleged that although this meeting was facilitated

by Novo Nordisk its sponsorship was not declared on the conference agenda. Novo Nordisk also had a promotional stand at the meeting; three of its sales representatives together with the sales manager attended the presentations and workshops which discussed incretin mimetics.

Lilly noted that in inter-company correspondence Novo Nordisk acknowledged that it 'helped fund the travel expenses of a visiting professor' and it also did not declare sponsorship of the meeting materials. This was attributed to error and the medical department not being told about the meeting.

Whilst the latter explanation offered no mitigation, Lilly queried Novo Nordisk's assertion that the professor was invited by the diabetes managed clinical network independently of Novo Nordisk. Lilly had it on good authority that the professor's input was facilitated by Novo Nordisk and that this included payment of an honorarium. This could be disclosed should it be required.

Lilly alleged that the professor's presentation 'Emerging New therapies in Diabetes Care' involved an unbalanced discussion of Byetta and liraglutide and invited a comparison of the two. In particular, reference was made to unpublished data from Novo Nordisk's Lead 6 study, a head-to-head comparison of Byetta and liraglutide. There was no clear indication of the licensed status of liraglutide and the impression created, by association to Byetta, was that liraglutide was available and a clinically relevant treatment option.

Lilly was also disappointed that both the speaker and Novo Nordisk disparaged Byetta throughout the presentation by referring to it as 'lizard spit'. Further, the discussion of Byetta was unbalanced and relatively abbreviated compared with that on liraglutide. To compound matters the speaker also stated that Byetta was only 50% homologous in comparison to human (physiological) GLP-1; although factually correct, the context in which this was discussed implied an inferior efficacy of Byetta. The speaker also inferred that liraglutide was developed later than Byetta because Novo Nordisk had deliberately taken longer researching this medicine in a more scientific way and hence liraglutide 97% homologous with human GLP-1; the implication being that Lilly had not conducted proper scientific research leading to the development of inferior products such as Byetta.

This presentation and the attendant workshop represented the pre-licence and disguised promotion of liraglutide which was further illustrated by the discussion of data comparing reduction of HbA_{1c} and weight loss data for Byetta and liraglutide. This was misleading as it implied, by association to Byetta, a licensed product, that liraglutide was also available and clinically relevant.

This activity constituted the pre-licence promotion of liraglutide, it invited misleading claims and comparisons with licensed medicines and constituted the disguised promotion of liraglutide. Lilly alleged breaches of the Code including Clause 2.

Lilly alleged that it was evident that Case AUTH/2202/1/09 did not represent an isolated instance of the pre-licence promotion of liraglutide by Novo Nordisk but was part of a concerted commercially driven objective. The above examples clearly demonstrated that Novo Nordisk had consistently, intentionally and widely promoted the availability of liraglutide in the UK prior to the grant of a marketing authorization. It was also evident that Novo Nordisk's medical and sales departments had not enforced the necessary standards with regard to compliance with the Code and also, on the company's own admittance, its internal policies and procedures.

In response to a request for further information Lilly stated that the undisclosed information it had regarding the honorarium paid to the professor was obtained from a managed care network which verbally confirmed that it had been paid £800 by Novo Nordisk to cover the professor's honorarium as a speaker. The managed care network then paid the professor.

Further, Lilly alleged that a Novo Nordisk sales representative transported the professor from the airport to the meeting and then on to another meeting; this was at odds with Novo Nordisk's position that the diabetes managed clinical network selected and invited the speaker entirely independently of the company.

The Panel noted that the professor's presentation included background information about GLP-1. A slide of a Gila Monster lizard was included and another slide headed 'GLP-1 analogues-available/in development' stated that Byetta came from Gila saliva. The next product mentioned on this slide was liraglutide with details that it was once daily. There was no distinction as to which medicines had marketing authorizations and which did not. Similarly a slide headed 'Efficacy of incretin therapeutics' unfavourably compared HbA_{1c} and body weight loss for Byetta with that for liraglutide and included FPG decreases and HbA_{1c} reductions for Januvia (sitagliptin) and Galvus (vildagliptin). The only product that did not have a marketing authorization was liraglutide and again no mention of this difference was made in the slides. Two other slides showed statistically significant advantages for liraglutide over exenatide in reduction of HbA_{1c} and improvement in beta-cell function over 26 weeks. The final slides referred to the pipeline for type 2 diabetes therapy.

The Panel was extremely concerned about the arrangements for Novo Nordisk's involvement in this meeting. It was not clear from Novo Nordisk's submission whether it had paid travel expenses only or paid an honorarium as alleged by Lilly. The role, if any of a Novo Nordisk representative in

providing/facilitating transport to and from the meeting was not clear. The agenda did not refer to Novo Nordisk's sponsorship of the professor. It was unacceptable for this not to be made clear on the documentation. In this regard the Panel considered that high standards had not been maintained and a breach of the Code was ruled.

The Panel noted Novo Nordisk's submission that the meeting was arranged by the diabetes managed clinical network which had selected and invited the speaker entirely independently of Novo Nordisk. However Novo Nordisk had contributed to the costs of the professor. Companies could not fund or otherwise facilitate a speaker as a means of avoiding the requirements of the Code. Given the title of the professor's presentation 'Emerging New Therapies in Diabetes Care' and the role of Novo Nordisk, it should have seen the materials prior to the presentation. The Panel was also concerned that Novo Nordisk was unsure as to where the professor had obtained Novo Nordisk unpublished material. Novo Nordisk should have checked the position with its head office.

Taking all the circumstances into account the Panel considered that, given Novo Nordisk's role, the sponsored presentation in effect promoted an unlicensed medicine. Thus a breach of the Code was ruled. This was disguised promotion and the material was misleading and included misleading comparisons. High standards had not been maintained. Breaches of the Code were ruled.

The Panel noted that Novo Nordisk had facilitated the professor's attendance and that he had somehow been given access to the company's unpublished data on file. The company's association with the speaker should have been made clear to the delegates. Novo Nordisk's omission in this regard reduced confidence in and brought discredit upon the industry. A breach of Clause 2 was ruled.

The Panel was extremely concerned that Novo Nordisk had promoted a medicine prior to the grant of its marketing authorization on a number of occasions. There appeared, in general, to be a poor understanding of the requirements of the Code. Novo Nordisk had acknowledged that its procedures were lacking; communication at all levels within the company was inadequate. The Panel considered that the circumstances warranted reporting Novo Nordisk to the Appeal Board for it to consider the matter in accordance with Paragraph 8.2 of the Constitution and Procedure.

The Appeal Board was extremely concerned about this case; the promotion of a medicine prior to the grant of its marketing authorization was a serious matter and displayed a poor understanding of the requirements of the Code. As well as being prohibited by the ABPI Code, it was also prohibited by the EFPIA Code on the Promotion of Prescription Only Medicines to, and Interactions with, Health Professionals. Headquarters staff in Denmark should know about the EFPIA Code. According to Novo Nordisk the website had been subjected to regulatory and legal review. The Appeal Board was not convinced that Novo Nordisk fully understood the seriousness of the matter and was especially concerned to note that the company had recently been found in breach of the Code for promoting liraglutide prior to the grant of its marketing authorization (Case AUTH/2202/1/09).

The Appeal Board noted that as a result of the rulings in this case Novo Nordisk had instigated a major review of its compliance systems, procedures and training. Code training of headquarters' staff was soon to be conducted by teleconference although the Appeal Board queried whether this was an effective training medium, given the seriousness of the case. The Appeal Board was very concerned about the apparent lack of influence that Novo Nordisk in the UK had over its headquarters in Denmark regarding compliance of material which came within the scope of the UK Code.

The Appeal Board decided in accordance with Paragraph 11.3 of the Constitution and Procedure to require an audit of Novo Nordisk's procedures in relation to the Code to be carried out by the Authority. The audit should be conducted as soon as possible. The Appeal Board suggested that relevant staff from Denmark should be interviewed. On receipt of the audit report the Appeal Board would consider whether further sanctions, including a report to the ABPI Board of Management, were necessary. In addition the Appeal Board decided that Novo Nordisk should be publicly reprimanded.

Upon receipt of the October 2009 audit report the Appeal Board was very concerned that as demonstrated in the audit reports of 2004/05 and the current audit report, Novo Nordisk clearly lacked processes to ensure compliance with the Code. This must be a priority for all including senior staff who must take more personal responsibility. The company must be able to show that this time it could change and develop attitudes and procedures which gave strong support to compliance.

The Appeal Board noted that Novo Nordisk was due to roll out a number of new standard operating procedures (SOPs) with training on them to commence early in 2010. This timeframe had been extended since the audit. The Appeal Board decided in accordance with Paragraph 11.3 of the Constitution and Procedure to require a further audit of Novo Nordisk's procedures in relation to the Code to be carried out by the Authority. The audit should be conducted in March 2010 when the Appeal Board expected Novo Nordisk's awareness of the Code and processes including the SOPs to be much improved and more embedded within the company. The re-audit in this case would take place at the same time as the audit required in Case AUTH/2269/9/09. On receipt of the audit report the Appeal Board would decide if further

sanctions were necessary.

Upon receipt of the March 2010 audit report the Appeal Board considered that Novo Nordisk's progress was not sufficiently rapid. It still had serious concerns about the company's approach and attitude to the Code. There were still significant problems with certification. Not all the standard operating procedures (SOPs) had been completed and trained out. This was now due to happen at the May sales conference (other than the SOP for medical and educational goods and services).

Overall, the Appeal Board considered that Novo Nordisk still did not appear to appreciate the seriousness of the situation. The Appeal Board considered requiring Novo Nordisk to submit material for pre-vetting as set out in Paragraph 11.3 of the Constitution and Procedure and/or report the company to the ABPI Board of Management. The Appeal Board decided to require another audit in June/July. On receipt of that audit report the Appeal Board would decide whether further sanctions, such as pre-vetting and/or a report to the ABPI Board were necessary.

Upon receipt of the July 2010 audit report the Appeal Board was concerned that it had taken some time but considered that significant progress had now been made. This must be maintained. The Appeal Board considered carefully all the options available noting that it had already decided that both cases (Cases AUTH/2234/5/09 and AUTH/2269/9/09) should be the subject of a public reprimand. It decided that no further action was necessary.

Eli Lilly and Company Limited alleged that Novo Nordisk Limited had promoted Victoza (liraglutide) prior to the grant of its marketing authorization.

Lilly's product Byetta (exenatide) was licensed for the treatment of type 2 diabetes mellitus in combination with metformin and/or sulphonylureas in patients who had not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.

Lilly was disappointed that despite the recent ruling in relation to the pre-licence promotion of liraglutide (Case AUTH/2202/1/09), Novo Nordisk apparently continued to disregard both the spirit and tenet of the Code and engaged in the pre-licence promotion of liraglutide, as evidenced by a number of activities.

* * * * *

Novo Nordisk advised that Victoza had been granted a marketing authorization on 30 June 2009.

Victoza was licensed to treat type 2 diabetes mellitus firstly in combination with metformin or a sulphonylurea in patients with insufficient glycaemic control despite maximal tolerated dose of monotherapy with metformin or sulphonylurea. Secondly, in combination with metformin and a sulphonylurea or a thiazolidinedione in patients with insufficient glycaemic control despite dual therapy.

The items at issue were as follows.

1 Educational website – 'Realising the promise of the GLP-1 receptor'

Lilly wrote to Novo Nordisk and 20 November 2008, concerned about the pre-licence promotion of liraglutide in the online Training Module developed by Novo Nordisk entitled 'Latest Advances in the Treatment and Management of Type 2 Diabetes – The Incretins'. As Novo Nordisk agreed to remove reference to liraglutide from the training module, Lilly did not complain about this matter in Case AUTH/2202/1/09.

Lilly was therefore disappointed, that a similar educational resource sponsored by Novo Nordisk was currently available online and once again, in the guise of educational material, involved the pre-licence discussion and promotion of liraglutide.

COMPLAINT

Lilly alleged that the primary objective of this website was to facilitate the pre-licence promotion of liraglutide and noted that a screen which it accessed on 23 April 2009 stated 'Thank you for registering with Liraglutide online!' and appeared when the 'New User Registration' hyperlink was activated.

In inter-company correspondence, Novo Nordisk stated that the screen '... was quite clearly, an oversight' and that 'measures will be implemented as soon as possible', instead of immediately, to address this. Lilly refuted the suggestion that this was an unintentional error; the wording 'Thank you for registering with Liraglutide online!' clearly demonstrated Novo Nordisk's intent to use the training module as a platform upon which to base pre-licence promotion of liraglutide. The removal of this wording did not negate Lilly's allegation that this website constituted the pre-licence promotion of liraglutide.

Lilly alleged that Module 4 ('Anti-diabetic strategies based on the incretin hormone system'), (ref UK/LR/0508/0011) invited a broad range of discussion and comparison of the efficacy and safety of various treatment strategies, some of which were licensed and some in development, such as liraglutide, and therefore unlicensed.

Section 3 of Module 4 (ref UK/LR/0508/0011; 'Available treatment options for type 2 diabetes based on the incretin hormone system'), misled readers as they were not informed which treatments within the classes discussed were currently available/licensed; a previous reference to 'learning outcomes' suggested that the provision of

this type of important information would be implicit given the title of this particular section. Therefore, given that liraglutide featured prominently in this online resource, to omit early clarification of its unlicensed status misled readers not only by omission but also by association ie discussion of liraglutide alongside licensed treatments in the class such as Byetta.

Section 4.1 of Module 4 (ref UK/LR/0508/0011) presented, in brief, an 'Overview and therapeutic indications' of Byetta. It was correctly stated that exenatide was first approved for the treatment of type 2 diabetes in 2005 and was now available for this purpose in many countries around the world. However, Lilly alleged that it failed to clarify to the reader that exenatide was the only licensed and available GLP-1 receptor agonist; this omission was intentional and misled the reader regarding the place of liraglutide, as a treatment option which was discussed extensively in Module 4.

Section 4.2 of Module 4 (ref UK/LR/0508/0011) was titled 'Liraglutide' in large emboldened font and provided an extensive discussion of the efficacy of liraglutide and information about clinical trials with comparators including metformin. This was further elaborated and reiterated in the 'Knowledge Tests' associated with the module thereby further maximising the opportunity to promote liraglutide pre-licence.

Lilly noted that it was only at the end of Section 4.2.1 titled 'Overview' that the statement 'Liraglutide is not yet licensed in the UK' appeared in very small font such that it was almost obscured. Lilly alleged that this did not however mitigate the substantive issue in question, which was the provision of pre-licence information on liraglutide.

Importantly, Lilly alleged that the format and layout of Module 4 intentionally misled by implication and invited a direct and misleading comparison of liraglutide with Byetta.

Lilly alleged that the efficacy and clinical trials information presented for liraglutide effectively invited a comparison of the efficacy of liraglutide in relation to Byetta and its licensed indication; the implication invited was that it was fair, balanced and legitimate to promote a comparison of an unlicensed medicine with one that was. This comparison was not only unfair and inappropriate but was unbalanced in favour of liraglutide given the abbreviated nature of the Byetta section of the module in comparison with that detailing liraglutide information.

Lilly alleged that this was further highlighted in Section 4.2.2 ('Effects on blood glucose control') which discussed the 'Effectiveness of liraglutide versus placebo and comparator drugs'. Table 3 referred to comparative HbA_{1c} data from the Lead 2 and Lead 5 clinical studies. The reader was indirectly invited to also compare the HbA_{1c} values for Byetta provided earlier in the module; any such comparison of liraglutide with Byetta was not based on a direct head-to-head comparison and was therefore misleading, unfair and unsubstantiated.

Lilly alleged that comparisons with other GLP [glucagon – like peptide] -1R agonists in development were presented in Section 4.3 alongside the statement '…even those agents still in preclinical development will not be available for prescription at present or in the near future'. Interestingly, this statement was not applied to liraglutide despite its clear applicability and relevance. The wording intentionally invited a comparison with liraglutide and suggested that liraglutide was a more clinically relevant choice given its implied availability. Indeed, in inter-company correspondence Novo Nordisk appeared to validate the discussion of liraglutide alongside products in preclinical development because liraglutide 'is in clinical development, not preclinical development.' This clearly demonstrated Novo Nordisk's failure to understand that the pre-licence discussion of liraglutide in a promotional website was not acceptable regardless of the development stage of the medicine.

Lilly noted that Sections 7 and 7.1 (ref UK/LR/0508/0011) of Module 4 discussed the tolerability and safety considerations of GLP-1 receptor agonists. Lilly failed to comprehend the relevance of any safety consideration of an unlicensed medicine such as liraglutide particularly when it invited a comparison with the safety profile of Byetta and other licensed treatments. Lilly alleged that given the latter, of particular concern was the unbalanced, alarmist and disparaging nature of the information and claims made in support of the safety profile of liraglutide in comparison with Byetta. For example, the promotional tone of the statement 'liraglutide [like all GLP-2 receptor agonists] is also associated with an increased incidence of nausea and other gastrointestinal side effects relative to placebo. Again, however, these are usually mild, transient, and infrequently associated with treatment discontinuation.', was in stark contrast to those about safety issues related to Byetta treatment; the latter drew attention to ' ... a high incidence of hypoglycaemia ...', 'A review of 30 cases of acute pancreatitis in patients receiving exenatide led to the addition of information relating to the risk of pancreatitis to the precautions section of the prescribing information of this product in January 2008'. Why had Novo Nordisk not employed an equally rigorous approach to providing equally relevant details clarifying the licensed status of liraglutide?

Lilly alleged that the 'Self-assessment' section associated with Module 4 could have afforded the opportunity to address the latter glaring omission. Instead however, as evidenced by question 4, the assessment invited a consideration of the route of administration of liraglutide by asking the question 'GLP-1R agonists such as exenatide and liraglutide are peptides that are administered by ...'.

The latter invited the reader to be misled by implication, omission and association to Byetta that liraglutide was available and not unlicensed in the UK.

Lilly alleged that Module 3 ('The physiology of incretins') and its association with Module 4 of this website further exemplified the misleading and contrived promotion of the liraglutide safety profile by association and implication. Section 6.4 of the module (ref UK/LR/0508/0011; 'Blood glucose lowering by GLP-1 is safe and effective') discussed the safety of injecting GLP-1 infusions and stated that these were 'well tolerated' and 'The incidence of all-cause adverse events was similar for both the placebo'.

This was followed by Section 7 ('Implications for therapy') which stated that 'The clinical studies summarised previously show that administration of GLP-1 has the potential to normalise blood glucose in patients with type 2 diabetes. Finally, infusions of GLP-1 given over three periods of a few days to several months were well tolerated. These observations support the potential for using novel therapeutic agents that act via GLP-1 receptors as monotherapy or within oral antidiabetic combination regimens. However, the extremely short survival of biologically active GLP-1 in the plasma renders treatment with GLP-1 itself impractical. Alternative strategies that exploit the incretin hormone system to deliver antidiabetic therapy are now available. These will be discussed in Module 4'.

Lilly also noted that the availability of this website was highlighted in the 'Resources and Support' section of Prescriber, 5 March 2009. Given the points above, Lilly alleged that promoting the availability of the website to the medical press effectively also supported the pre-licence promotion of liraglutide.

Lilly categorically refuted Novo Nordisk's assertion that this website was simply an educational resource. This activity constituted the pre-licence promotion of liraglutide, it invited misleading claims and comparisons with licensed medicines and represented the disguised promotion of liraglutide. Lilly alleged breaches of Clauses 3.1, 7.2, 7.3, 7.9, 8.1 and 12.1 of the Code and, given the serious nature of the matter, a breach of Clauses 9.1 and 2.

RESPONSE

Novo Nordisk submitted that the website in question was authored by an external agency. It was initiated by Novo Nordisk UK as an educational resource for health professionals to raise their awareness of the GLP-1 receptor, together with current and future therapies based around incretins. The web pages were approved and certified in accordance with the Code. The Code allowed educational activities, and Novo Nordisk submitted that this website complied with the Code, and was a useful resource for health professionals.

Novo Nordisk agreed that the statement 'Thank you for registering with Liraglutide online!' on the registration hyperlink page was unacceptable from the perspective of the Code and could be perceived as leading to a platform where there was pre-licensed promotion of liraglutide, which was not the case, once the site was entered. It therefore instructed the external agency to promptly remove this statement from the web page, which it did within 24 hours. Novo Nordisk rejected other allegations in the complaint made by Lilly regarding the website.

Novo Nordisk noted that the four modules of the educational website extensively discussed the following:

pathogenesis of type 2 diabetes mellitus (focusing on ß-cell failure) (Module 1); the potential advantages/disadvantages of the available antihyperglycaemic compounds other than incretin-based therapies (Module 2);
the physiology of the incretin system (Module 3) and incretin-based therapies (Module 4).

Liraglutide was first and only mentioned in Module 4 therefore its licence status was sufficiently clarified in the Overview section of this Module; namely Section 4.2.1 – the first section mentioning the compound.

The amount of scientific information relating to type 2 diabetes in the modules relative to the amount of information about liraglutide showed the commitment to create an important educational tool for health professionals interested in this therapy area. Lilly suggested that liraglutide featured prominently in this online resource, but had been covered only in the sections where this was relevant, such as where exenatide was discussed. Thus this suggestion was refuted.

Lilly alleged that Section 3 could mislead the readers in terms of the licence status of liraglutide, however Novo Nordisk submitted that the section in the link 'Click here to view descriptions of the therapeutic options' solely described the two classes of incretin-based therapies (DPP-IV inhibitors and GLP-1R agonists) without specifically mentioning any compound. Liraglutide was mentioned first in Section 4.

Lilly also alleged that Section 4.1 failed to highlight the fact that exenatide was the only licensed and available GLP-1 receptor agonist and this would mislead the readers in terms of the licence status of liraglutide. Again, liraglutide was not mentioned in this online educational tool by this point; it was first discussed in the next section. Since the next overview section had the statement which clarified that liraglutide had currently no marketing authorization in the UK, Novo Nordisk submitted that the lack of emphasis of the issue raised by Lilly would not mislead the reader as suggested.

Novo Nordisk submitted that the allegation that the sentence which highlighted the licence status of liraglutide could only be found at the end of Section 4.2.1 was true, however Lilly had failed to note that this was the first section discussing this compound, and as such, Novo Nordisk submitted this was the relevant part of Module 4 in which to emphasise this fact. The statement was in the same font as the rest of this paragraph and could not, as stated, be considered as 'very small font such that it is almost obscured'.

Lilly stated that the whole format and layout of Module 4 invited a direct and misleading comparison of liraglutide with Byetta. Novo Nordisk submitted that such comparisons would not have any meaningful scientific grounding and health professionals were also aware of this. Therefore Lilly's allegation suggested that health professionals did not know how clinical trial results should be compared in a scientific way; this was discourteous to clinical colleagues.

Novo Nordisk submitted that it was important to highlight that the out of context emphasis in Lilly's complaint and the suggestion that Novo Nordisk had discussed exenatide and liraglutide in an unfair, unbalanced way was unsubstantiated when viewing the material to which it referred as a whole. Lilly had alleged that liraglutide featured prominently in Section 3 of this online resource. In fact only Module 4 discussed liraglutide and provided exactly the same amount of information about it as it did about exenatide. In regard to Section 4.1 Lilly had alleged that Byetta was presented in brief whereas liraglutide was discussed extensively. In fact the structure of the sections where these agents were discussed were the same, in that they each provided exactly the same amount of information for each compound. Although Lilly had alleged that Section 4.2 was titled 'Liraglutide' in large emboldened font; Section 4.1 about exenatide was titled in exactly the same way. Novo Nordisk noted that Lilly had alleged that this comparison was not only unfair and inappropriate but was unbalanced in favour of liraglutide given the abbreviated nature of the Byetta section of the module compared with to that detailing liraglutide. Novo Nordisk was particularly disappointed about this view given that the structure of Module 4 provided the same amount of information on each compound.

Novo Nordisk submitted that Lilly's concern relating to Section 7 was unclear how it failed to understand that it was possible to provide safety data about a compound in the pre-licence period. Fortunately regulatory authorities acknowledged safety data from clinical trial phases of a medicine development program, and acknowledged that these programs served as a solid basis for any new licence approval.

Regarding Lilly's concern that information and claims made in support of the safety profile of liraglutide in comparison with Byetta were unbalanced, alarmist and disparaging, Novo Nordisk submitted that the quoted hypoglycaemia incidence rates were in Byetta's prescribing information and came from the most important randomized clinical trials Lilly had conducted with exenatide in the late phase of its clinical development programme. It was unfortunate that Lilly considered facts from its own prescribing information were disparaging.

Furthermore Novo Nordisk submitted that it was difficult to comprehend the relevance of comparing the 'promotional tone' used, according to Lilly, in the statement supporting liraglutide in terms of its gastrointestinal side effects to the safety issues relating to the treatment with Byetta regarding its hypoglycaemic risk profile and the risk of pancreatitis, which resulted in Lilly requesting a label change by the FDA in the Byetta prescribing information.

Novo Nordisk submitted although liraglutide was discussed in a fair and balanced way compared to exenatide only in Module 4 interestingly Lilly also considered Module 3 misleading and promotional in terms of the safety profile of liraglutide. In fact this module was about the physiology of incretins in general without mentioning any specific medicine. With regard to Lilly's particular concern about Section 6.4, this provided information about the safety profile of GLP-1 based blood glucose lowering therapy and referred to two publications published in Diabetes Care in 2001 and 2003. Both papers investigated biosynthetic GLP-1, hence any interpretation of the results should be equally relevant both in terms of exenatide and liraglutide. Thus Novo Nordisk denied that this section could be considered as disguised promotion of liraglutide. Novo Nordisk intended this section to provide useful scientific information for health professionals only, rather than to promote any specific medicine.

Novo Nordisk provided, in confidence, the agreement between it and the external agency which developed the educational website. The agreement clearly showed the intention to develop an online tool for non-promotional educational purposes. Novo Nordisk noted that Schedule 1 of the agreement showed that it clearly understood how liraglutide could be discussed before and after its marketing authorization had been granted.

Finally Novo Nordisk stated that there were 109 registered users of this website on 8 June 2009. The low number certainly did not indicate a lack of interest in the topic, but rather reflected the fact that Novo Nordisk had not promoted the availability of this website, and that it was primarily used as a reference for those health professionals who, in an unsolicited approach to Novo Nordisk, requested more information about GLP-1 based therapies from its medical information team.

Given the above Novo Nordisk categorically refuted the allegations that the education website facilitated the pre-licence promotion of liraglutide.

However, since this was the second time Lilly had tried to challenge the value of this educational tool alleging its promotional nature, Novo Nordisk had decided to close the website although it still believed it was a valuable source of information for health professionals.

PANEL RULING

The Panel noted that, in its response to the Authority, Novo Nordisk had stated that it had decided to close the website at issue. Lilly had not been notified. The Director considered, however, that in the circumstances inter-company dialogue had not been successful. The Panel considered the case.

The Panel noted that the Code permitted certain activities prior to the grant of a marketing authorization. The supplementary information to Clause 3 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 prohibited under Clause 3 or any other clause.

In the Panel's view the closer the grant of the marketing authorization for a product the more difficult it was to argue that activities constituted the legitimate exchange of medical and scientific information during the development of a medicine and were not promotion. The marketing authorization for Victoza was granted on 30 June 2009.

The Panel noted Novo Nordisk's submission that the website was an educational resource and queried whether providing such material about a product and its therapeutic area a few months before the grant of its marketing authorization would ever be acceptable under the Code given that the definition of promotion was any activity undertaken by a pharmaceutical company, or with its authority, which promoted the prescription, supply, sale or administration of its medicines. Obviously the content of such material would be important.

The Panel considered it was irrelevant how many users had registered to use the website as was the amount of information about liraglutide relative to other information.

The Panel was extremely concerned to see that following registration a message 'Thank you for registering with Liraglutide online!' appeared. This was compounded by the name of the website 'Realising the promise of the GLP-1 receptor.' The Panel considered that the first impression was not of an educational online resource but promotion of liraglutide as alleged. The Panel noted that Novo Nordisk had removed the reference to liraglutide. It did not appear on the version of the educational module provided by Novo Nordisk to the Authority. Nevertheless the Panel considered that the fact that such a reference had been included at all was of serious concern.

The Panel considered that it was misleading as alleged not to have made it clear that exenatide was the only licensed GLP-1 receptor agonist.

The Panel also considered that Section 4.2 would lead readers to compare exenatide and liraglutide. The comparative data presented for liraglutide did not include direct comparisons with exenatide which was not the impression given by the claim 'liraglutide was at least as effective as the comparator treatments in these trials'.

The separation between exenatide and liraglutide from other GLP-1R agonists which were described as being included for completeness and 'However unlike exenatide even those agents still in preclinical development will not be available for prescription at present or in the near future' further reinforced the impression that both exenatide and liraglutide were available for prescription. This was misleading.

Module 4 included many claims for similarities between exenatide and liraglutide or advantages for liraglutide. The Panel considered that this further added to the promotional nature of the material.

Section 7 on tolerability and safety considerations compared the profiles of exenatide and liraglutide. It referred to additions to the Byetta summary of product characteristics (SPC) in January 2008 to include the risk of pancreatitis. Byetta had received its marketing authorization in November 2006. The Victoza SPC referred to the risk of pancreatitis with other GLP-1 analogues and the need to discontinue Victoza and other potentially suspect medicinal products. The failure to include any of this information in the module was of concern particularly as it was not made clear that liraglutide did not have a marketing authorization and the difference in available information given that there was more experience with exenatide.

The Panel noted that Lilly's concern that statements about the safety profile of liraglutide went beyond the inclusion of the hypoglycaemia incidence rates from the Byetta SPC as submitted by Novo Nordisk.

The agreement with the external agency made it clear that the material on the website needed to comply with the ABPI Code among other regulations and codes.

The Panel was extremely concerned about the material in question. It included detailed information about liraglutide, a product that did not have a marketing authorization. The Panel considered that the material promoted liraglutide. In this regard the Panel noted the initial references to exenatide and the failure to be very clear about the differences in the regulatory status of the products. A breach of Clause 3.1 was ruled. The material was misleading and included misleading comparisons.

Breaches of Clauses 7.2 and 7.3 were ruled. The Panel ruled a breach of Clause 7.9 in relation to the section on tolerability and safety. The Panel did not consider the material disparaged Byetta and no breach of Clause 8.1 was ruled. The material was disguised promotion and a breach of Clause 12.1 was ruled. High standards had not been maintained and a breach of Clause 9.1 was ruled.

The Panel noted that promoting a medicine prior to the grant of the marketing authorization was an activity that was listed in the supplementary information as an activity likely to be in breach of Clause 2 of the Code. That clause was used as a sign of the particular censure. The Panel ruled a breach of Clause 2.

2 Sponsored supplement in The British Journal of Diabetes & Vascular Disease, November/December 2008, Volume 8 Supplement 2

The front cover of the above supplement, 'The Modulating Effects of GLP-1 in Type 2 Diabetes: Proceedings from a symposium of the 43rd Annual Meeting of the European Association for the Study of Diabetes [EASD] Amsterdam, The Netherlands, 17 September 2007' stated 'This supplement has been supported by an educational grant from Novo Nordisk'. Lilly alleged that the supplement was being used promotionally by Novo Nordisk as evidenced by its distribution in the UK with The British Journal of Diabetes & Vascular Disease, January/February 2009, Volume 9 Issue 1.

COMPLAINT

Lilly alleged that the above title and reference of the 43rd Annual Meeting of the EASD misleadingly implied that the supplement was an independent report of the proceedings from this meeting and not in fact those from a closed promotional satellite symposium run by Novo Nordisk. This was further compounded by the format and layout of the supplement which suggested it was a part of and integral to the accompanying medical journal. The statement 'This supplement has been supported by an educational grant from Novo Nordisk' as it appeared on the cover disguised the promotional nature of the material, which was in fact a paid for insert detailing the proceedings of a company meeting which involved the pre-licence promotion of liraglutide. The concept of the insert and its content was clearly derived and editorially controlled by Novo Nordisk and represented the outputs from its satellite symposium.

On page S1, the author, who chaired the Novo Nordisk satellite symposium introduced the five articles and stated 'Agents such as the GLP-1 receptor agonist exenatide and the DPP-4 inhibitors sitagliptin and vildagliptin are now available (the latter not in the USA) for utilisation in regimens to treat type 2 diabetes, while the GLP analogue liraglutide may soon be available'.

Lilly alleged that the unlicensed status of liraglutide was not clearly stated and that its availability was underplayed relative to the wording adopted for vildagliptin. Lilly noted that it was only here that the derivation of four of the five articles was explained, albeit briefly, and linked to '… a symposium held on 17 September 2007, during the European Association for the study of Diabetes Meeting in Amsterdam'; although the fact that it was sponsored by Novo Nordisk was conveniently omitted.

Lilly noted that on pages S10 – S18 the article 'Pharmacology of GLP-1 based therapies' discussed liraglutide clinical trial data and stated that 'Liraglutide is a once-daily human GLP-1 analogue with high (97%) sequence identity'. Lilly alleged that this wording implied a licensed posology for liraglutide. The article went on to make pre-licence promotional claims in support of the pharmacokinetics, pharmacodynamics, mode of action and clinical efficacy of liraglutide and invited the reader to consider the 'clinically relevant reductions in HbA_{1c} compared to placebo, without hypoglycaemia and with weight loss of up to 3kg'. Again, the author highlighted the licence status of vildagliptin by stating 'DPP-4 inhibitors, such as vildagliptin (not available in the USA) ...' but failed to clarify that liraglutide was not licensed in the USA or in Europe; thus misleading by omission and suggesting, by association, that all the other GLP-1 based therapies mentioned were in fact licensed.

Lilly noted that on pages S19 – S25 the article 'Managing the ß-cell with GLP-1 in type 2 diabetes' discussed preclinical and clinical data in the pre-licence promotion of liraglutide for the treatment of type 2 diabetics.

Lilly alleged that a common theme in this insert was to misleadingly associate the discussion of liraglutide alongside licensed treatments such as Byetta. This was clearly demonstrated in a section entitled 'GLP-1 treatment in type 2 diabetes' where Byetta was discussed as 'The first GLP-1 analogue available …' This was then directly followed by the statement 'A second GLP-1 analogue is liraglutide. In the development of liraglutide ...' thus creating the misleading impression that liraglutide had already been developed and should be regarded in the same context as Byetta, a licensed treatment.

Given all of the above points Lilly alleged that the article on pages S26 – S33, 'Liraglutide, a once-daily human GLP-1 analogue' evidenced the significant extent to which liraglutide was discussed at the Novo Nordisk satellite symposium. Indeed, the article authored by the meeting chairman also made pre-licence promotional claims in support of the efficacy and safety of liraglutide. The abstract section stated 'The effects of liraglutide are maintained over 24h, allowing daily dosing. Liraglutide provides all of the beneficial actions of endogenous GLP-1: glucose dependant stimulation of insulin secretion, glucagon suppression, deceleration of gastric emptying, appetite

suppression/weight loss …', '... the risk of treatment-associated hypoglycaemia is low.', 'in clinical studies, liraglutide substantially lowered fasting and postprandial glucose concentrations, with an overall reduction in haemoglobin A_{1c} of up to 1-2%. In some studies liraglutide decreased several biomarkers of cardiovascular risk and lowered triglyceride levels significantly'.

Again, Lilly alleged that there was no explicit clarification that liraglutide was not licensed in the UK. Given the latter, the detailed discussion of liraglutide over the next six pages, which included the long-term effects of liraglutide on progression of type 2 diabetes (remarkable for a medicine that was not yet licensed!), clearly invited the suggestion that liraglutide was clinically relevant in the treatment of type 2 diabetes and available. This impression was reinforced in the 'Key messages' box which reiterated the messages that 'Liraglutide is a once-daily GLP-1 analogue that has a promising clinical profile including substantial improvement in glycaemic control without a risk for hypoglycaemia, and weight loss as an added benefit'.

Lilly alleged that on pages S34 – S41 an article 'Mechanisms behind GLP-1 induced weight loss' invited a discussion of liraglutide data and its effect on weight loss, and by reference to licensed medicines such as exenatide and sitagliptin invited the reader to consider it as 'a desirable option for the treatment of type 2 diabetes, as [it] improves[s] glycaemic control, improve[s] pancreatic function and induce[s] clinically meaningful weight loss' and its '…potential to modify type 2 diabetes disease progression'.

Lilly also noted that, unlike the preceding four articles, this one was not from the Novo Nordisk satellite symposium but did involve editorial input from a Novo Nordisk employee as evidenced by the 'Acknowledgements' which stated 'The author has received many helpful comments to the manuscript from [a named doctor] ...'; this being the same senior specialist from Novo Nordisk referred to in point 3 below.

In conclusion, Lilly alleged that presenting the output of a Novo Nordisk run meeting as an independent supplement to a journal demonstrated apparent poor knowledge of the requirements of the Code. Health professionals generally looked to medical journals as a source of independent information therefore Novo Nordisk should have made it clear that the authors wrote the articles on behalf of and as a result of its promotional activities.

Lilly alleged that the misleading description and presentation of this insert and its pre-licence promotion of liraglutide represented a breach of the Code.

Lilly did not accept the assertion that 'Due to the fact that Novo Nordisk had no input into this item, we do not feel able to comment on the specific issues raised in your letter'. The Novo Nordisk response during inter-company correspondence regarding this paid insert clearly acknowledged that both Novo Nordisk and its parent company disregarded the requirements of the Code with respect to promotional activities undertaken within the UK.

Lilly alleged that this activity constituted the pre-licence promotion of liraglutide, it invited misleading claims and comparisons with licensed medicines and represented the disguised promotion of liraglutide in breach of Clause 3.1, 7.2, 7.3, and 12.1 and, given the serious nature of the matter, breaches of Clauses 2 and 9.1.

RESPONSE

Novo Nordisk referred to inter-company dialogue in which it submitted that the supplement was initiated by its corporate offices in Denmark, in association with the USA affiliate. Within Novo Nordisk, there was a very clear standard operating procedure which stated that all material to be published in the UK, or for a UK audience, needed to be approved by the UK affiliate for Code compliance. Unfortunately, it appeared that the supplement in question was not sent to the UK for approval. Novo Nordisk was currently looking into re training its corporate offices and was taking steps to ensure that similar activities could not occur in the future.

Novo Nordisk submitted that Lilly was incorrect to claim that the supplement had been used promotionally. The supplement had not been issued directly to any health professional by any Novo Nordisk employee, had not been displayed on any promotional stand and had not been quoted from in any promotional material. In addition, Novo Nordisk had not used the supplement internally for training/education purposes.

Due to the fact that Novo Nordisk had no information about, and no input into the supplement in question it was unable to comment on the specific issues raised by Lilly.

In response to a request for further information Novo Nordisk confirmed that the supplement reflected the programme of a satellite symposium organised by Novo Nordisk in Amsterdam, September 2007, before the annual meeting of the EASD. However Novo Nordisk did not understand the concern regarding the layout of the supplement. This supplement was an official supplement to the British Journal of Diabetes & Vascular Disease, which was supported by a grant from Novo Nordisk (Novo Nordisk's funding role was highlighted on the front page of the journal). The fact that this was a paid supplement did not mean a different layout was required. In fact, such a supplement should be an integral part of the journal itself.

To Novo Nordisk's knowledge, save for the last paper, the content of the supplement was written by

the speakers of the symposium with no editorial input from Novo Nordisk. As was acknowledged by Lilly, the last paper was not derived from the symposium. It discussed GLP-1-induced weight loss from a general GLP-1 perspective and mentioned both exenatide and liraglutide in one single sentence respectively. The contribution by the Novo Nordisk's scientist was sufficiently emphasised in the acknowledgement at the end of the paper. Thus Novo Nordisk UK did not believe the last paper promoted liraglutide.

Novo Nordisk also did not believe Holst *et al* promoted liraglutide. This paper discussed the pharmacology of GLP-1-based therapies. The allegation that the paper discussed liraglutide clinical data and made pre-licence promotional claims was incorrect. In the main, the paper discussed the pharmacological effects of the native GLP-1 molecule (equally relevant from exenatide and liraglutide perspectives). The first paragraph on page S15 which was about a specific incretin-based compound rather than GLP-1 in general, actually discussed exenatide. In fact readers could find more clinical data in relation to trials on exenatide rather than clinical data relating to liraglutide. There was in fact only a small paragraph which mentioned liraglutide as one of the albumin-based GLP-1 analogues, in contrast to the remainder of this page which discussed Lilly's products (both licensed and unlicensed). The author also discussed exenatide LAR and provided comparable amounts of data about this future compound by Lilly as he provided about liraglutide. Novo Nordisk noted that the author explicitly stated that liraglutide was in the development phase ('Three compounds using different methods to achieve this are in development'). Furthermore Lilly referred to a quotation from the abstract 'clinically relevant reductions in haemoglobin A1c compared with placebo, without hypoglycaemia and with weight loss of up to 3kg', and donated this phrase as relating exclusively to liraglutide and hence a pre-licence promotional claim. However when this quotation was read in the context of the paper as a whole, it could be seen that the author actually related this statement to both exenatide and liraglutide.

The intention of the prominent authors of this whole supplement was to provide a useful educational source of balanced scientific information about GLP-1 based therapies. Novo Nordisk did not believe that when the supplement was read in its entirety that it would be considered as a promotional article in relation to liraglutide or at all.

However Novo Nordisk realised there was a failure in its internal review process relating to approval of this UK-based journal supplement by the UK affiliate. Its new legal and compliance team was currently addressing this issue with relevant colleagues from Novo Nordisk headquarters in Copenhagen in order to improve this internal procedure.

PANEL RULING

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

The Panel noted that the objectives of the material in question, 'The Modulating Effects of GLP -1 in Type 2 Diabetes', was to provide the proceedings of a symposium, sponsored by Novo Nordisk at an international meeting, in the form of a journal supplement. The Panel considered that it would not always be possible to achieve this and comply with the requirements of the Code. Within the context of an international conference, attended by thought leaders, investigators and the like, it was possible for pharmaceutical companies to hold symposia about unlicensed products or indications as long as such activities were not otherwise promotional. The Code did not prohibit the legitimate exchange of medical and scientific information during the development of a medicine provided such activity was not promotion which was prohibited under Clause 3 or any other clause. The unsolicited distribution of symposia proceedings by a pharmaceutical company to health professionals who had not attended the meeting was not acceptable if the material referred to unlicensed medicines or did not otherwise comply with the Code.

The Panel noted that the supplement had been initiated by Novo Nordisk and its agency. The authors were mostly those who had taken part in the company sponsored symposium.

The Panel considered that Novo Nordisk was inextricably linked to the production of the supplement. There was no arm's length arrangement between the provision of the sponsorship and the generation of the supplement. Circulation was not limited to those who attended the Novo Nordisk sponsored meeting as it was circulated with The British Journal of Diabetes & Vascular Disease in the UK. The Panel noted that it was an established principle under the Code that UK companies were responsible for the activities of overseas affiliates that came within the scope of the Code. Thus Novo Nordisk UK was responsible under the Code for the distribution in the UK. Given the company's involvement and the content of the supplement, the Panel considered that the supplement was, in effect, promotional material for

liraglutide. The Panel considered that the material was a paid-for insert from Novo Nordisk, not a supplement from The British Journal of Diabetes & Vascular Disease for which the journal's editorial board would have been responsible. The insert was distributed with The British Journal of Diabetes & Vascular Disease when liraglutide did not have a UK marketing authorization. The Panel considered that the insert promoted liraglutide to UK health professionals prior to the grant of its marketing authorization. A breach of Clause 3.1 was ruled.

The insert gave the misleading impression that liraglutide was licensed and this was not so. A breach of Clause 7.2 was ruled. The insert also invited the reader to make misleading comparisons about the licensed status of GLP-1-based therapies as alleged. A breach of Clause 7.3 was ruled. The insert gave the impression that it was a report of an independent meeting. The Panel considered that the insert was disguised promotion and a breach of Clause 12.1 was ruled. The Panel considered that the role of Novo Nordisk was not clear. It was misleading to merely state that the insert had been supported by an educational grant from Novo Nordisk when the meeting was a Novo Nordisk sponsored symposium. The Panel considered that high standards had not been maintained and a breach of Clause 9.1 was ruled.

The Panel considered that presenting the output of a Novo Nordisk meeting as an independent supplement to a journal demonstrated apparent poor knowledge of the requirements of the Code. Health professionals generally looked to medical journals as a source of independent information; where authors wrote on behalf of pharmaceutical companies this must be clear. In the Panel's view the majority of readers would have viewed the material at issue quite differently if they had known that it was the report of a company sponsored meeting. The Panel considered that the description and presentation of the insert was such as to reduce confidence in, and bring discredit upon the pharmaceutical industry. A breach of Clause 2 was ruled.

3 Novo Nordisk Symposium on Diabetes Care, March 2009

Lilly stated that this promotional meeting, sponsored by Novo Nordisk, concluded with a 'Key Note Lecture' which was chaired by a senior clinical nurse specialist and included a one hour lecture/presentation 'A New Molecule in Diabetes – From Conception to Reality' delivered by a senior specialist, Novo Nordisk A/S.

COMPLAINT

Lilly alleged that this presentation involved the pre-licence discussion and promotion of liraglutide to health professionals. It appeared that Novo Nordisk had intentionally commercialised liraglutide by a keynote lecture to promote the product and create the misleading impression amongst the delegates that liraglutide was a licensed and relevant treatment option for the management of diabetes. This was evidenced by the context in which this particular lecture was presented ie preceded by an extensive discussion of subjects such as 'Diabetes – A Weighty Issue, New Treatments, Guidelines for Diabetes Care'.

In inter-company correspondence Novo Nordisk acknowledged that the keynote lecture by a Novo Nordisk employee focused on the development of liraglutide, hence the title 'From Conception to Reality'. Given the latter and the fact that this was clearly a Novo Nordisk sponsored promotional meeting, Lilly refuted Novo Nordisk's assertion that this meeting was 'a very useful educational meeting, rather than a promotional opportunity'.

Lilly alleged that this activity again constituted the pre-licence promotion of liraglutide, it invited misleading claims and comparisons with licensed medicines and represented the disguised promotion of liraglutide in breach of Clauses 3.1, 7.2, 7.3 and 12.1 and given the serious nature of the matter, breaches of Clauses 9.1 and 2.

RESPONSE

Novo Nordisk referred to inter-company dialogue in which it submitted that the symposium on diabetes care had been running for the past few years, and was widely regarded by attendees as a very useful educational meeting, rather than a promotional opportunity. The keynote lecture 'A New Molecule in Diabetes – From Conception to Reality' was delivered by a senior specialist at Novo Nordisk.

Novo Nordisk refuted Lilly's allegation that the aim of the keynote lecture was to promote liraglutide and create the misleading impression it was a licensed and relevant treatment option for the management of diabetes. The senior specialist clearly stated that liraglutide was not licensed. In addition, the topic of the presentation was the development of liraglutide, hence the title 'From Conception to Reality'; the senior specialist did not state or imply anything which could be perceived as promotional.

PANEL RULING

The Panel noted that Novo Nordisk was responsible for the meeting. The final presentation was the one at issue. The title 'A New Molecule in Diabetes – From Conception to Reality' implied that the new molecule (liraglutide) was available for use and this was not so. No details had been provided about the delegates. The Panel considered that the meeting would be considered as promotional given it was a Novo Nordisk meeting. The presentation by a Novo Nordisk employee needed to comply with the Code. The content referred to GLP-1 and its clinical potential as well as GLP-1 analogues. It included detailed information about liraglutide. The presentation compared liraglutide with exenatide,

vildagliptin, glimepiride, rosiglitazone and glargine. The last few slides compared liraglutide and exenatide in relation to HbA_{1c}, HOMA, body weight and frequency of nausea. Each parameter favoured liraglutide and the HbA_{1c} and HOMA data were statistically significant. The final slide showed advantages for exenatide compared with glargine in relation to a composite endpoint of $HbA_{1c} \leq 7.4\%$ and weight gain ≤ 1kg. There did not appear to be any mention of the licensed status of the product. The final slide concluded that GLP-1 based therapies were highly interesting for treatment for type 2 diabetes and that GLP analogues might be made once daily treatments.

The Panel considered that taking all the circumstances into account the keynote presentation constituted promotion of liraglutide at a time when it did not have a marketing authorization. Thus the Panel ruled a breach of Clause 3.1 as alleged. The title of the presentation was misleading. A breach of Clause 7.2 was ruled. The presentation included comparisons with licensed medicines and could be seen as taking unfair advantage of the reputation of licensed medicines thus a breach of Clause 7.3 was ruled. The Panel did not consider that the meeting constituted the disguised promotion of liraglutide. The presentation was clearly promotional and no breach of Clause 12.1 was ruled.

The Panel considered that high standards had not been maintained and ruled a breach of Clause 9.1. The Panel noted that promoting a medicine prior to the grant of the marketing authorization was an activity likely to be in breach of Clause 2. That clause was used as a sign of particular censure. The Panel ruled a breach of Clause 2.

4 An endocrine and diabetes society meeting, February 2009

Lilly was aware that Novo Nordisk in partnership with an endocrine and diabetes society was developing local research strategy involving collaboration between centres throughout the local area. To support this, a senior member of Novo Nordisk's sales department helped convene/facilitate the above company sponsored meeting which included discussion of liraglutide data in diabetes and obesity, the latest Levemir (insulin detemir) data, ongoing development/ research projects and opportunities for collaboration in areas of pharmacological research in the local area amongst other things. Novo Nordisk extended an open invitation for any health professionals interested in participating in collaborative research projects to attend.

COMPLAINT

Lilly alleged that this was clearly a promotional meeting sponsored by Novo Nordisk as evidenced by the tacit and direct involvement of sales and marketing staff; this was acknowledged by Novo Nordisk in inter-company correspondence. Lilly failed to understand why a member of the sales department would be involved in a meeting purporting to be focused on the information needs of 'potential and existing investigators' and where the objective was 'to update [delegates] on current and future research projects'.

Lilly alleged that the discussion of liraglutide data and other medicine development/research projects and data constituted pre-licence disguised promotion of liraglutide in breach of Clauses 3.1 and 12.1 and given the serious nature of the matter, breaches of Clauses 9.1 and 2.

RESPONSE

Novo Nordisk referred to inter-company dialogue in which it submitted that the meeting at issue was initiated by the endocrine and diabetes society which asked the senior member of its sales department for an update on ongoing and future research activities at Novo Nordisk. This request was forwarded to the clinical research department as it had strong links with the endocrine and diabetes society. Invited delegates were potential and existing investigators, and the aim of the meeting was to update them on current and future research projects within Novo Nordisk. With this in mind, it was entirely appropriate to talk about liraglutide data, latest Levemir data and other ongoing development/research projects, as it was made clear both by the purpose of the meeting and the individual presentations that this was an update on research and at no point were any promotional claims made, either directly or indirectly.

Novo Nordisk submitted that however, during the planning phase of this meeting, the clinical research department invited the senior member of the sales department to attend, purely in an observational role; he had no input into the content of the meeting, and did not take an active role at any point during the meeting. All parties had been reminded of the importance of the Code with relation to sales/marketing involvement and attendance at meetings where pre-licence or off-licence data was to be discussed.

Novo Nordisk provided a copy of a letter from the endocrine and diabetes society received after Novo Nordisk submitted its response on 22 June. Novo Nordisk submitted that this further confirmed that the meeting was not a Novo Nordisk initiative and Novo Nordisk did not have any intention to utilise it as a promotional platform.

PANEL RULING

The Panel noted that few details had been provided about this meeting. A presentation about 'On going development projects' had been given. The meeting appeared to have been held in response to an unsolicited request from the endocrine and diabetes society for an update on ongoing and future research projects. From the agenda all of the

speakers were from Novo Nordisk. The Panel was concerned that a senior member of the company's sales department had attended, albeit by invitation. The impression that that gave was important.

The Panel examined the slides used by Novo Nordisk for the presentation 'On going development projects'. The introduction referred to insulin research and development including future insulins and products Novo Nordisk was working on. It also referred to GLP-1 development. Information was presented about a study on islet transplantation which ran from April 2009.

The Panel was concerned that based on Novo Nordisk's activities already considered above, in particular points 1 and 2, it was possible that liraglutide had been promoted to the audience. The Panel considered that this meeting appeared to be different to the one at issue in point 3 above in that it was organised by Novo Nordisk in response to a request that the meeting be held. However the complainant had the burden of proving their complaint on the balance of probabilities. The Panel considered that given all the circumstances and the limited evidence before the Panel, the meeting could be regarded as the legitimate exchange of scientific information. Delegates were invited as potential or existing investigators, not as prescribers per se. No breach of Clauses 3.1 and 12.1 was ruled. The Panel also ruled no breach of Clauses 2 and 9.1.

5 Diabetes network meeting, March 2009

COMPLAINT

Lilly alleged that this promotional meeting sponsored by Novo Nordisk invited presentations and discussions about the management of patients with type 2 diabetes and presented information and various data about liraglutide, which, at the time, was unlicensed in the UK. A significant part of the meeting was devoted to a debate 'This house believes that GLP-1 agonists (such as exenatide and liraglutide) are the best second line therapy for type 2 diabetes'.

Further, Lilly alleged that the debate involved the presentation of liraglutide data to health professionals and engaged the audience in the pre-licence discussion of liraglutide and its place in the management of type 2 diabetes alongside licensed GLP-1-based therapies such as Byetta; this was misleading by implication as it implied that liraglutide was a licensed and relevant treatment option for the management of diabetes. The meeting was attended by Novo Nordisk sales representatives, which further exemplified the promotional nature of this meeting. Discussion of liraglutide, directly or indirectly, at this meeting was of commercial interest to Novo Nordisk.
Lilly alleged that reference to topics on new treatment options in diabetes, the incretin system, modulators or mimetics of GLP-1, GLP-1 receptor agonists and the dipeptidyl IV receptor antagonists, effectively solicited questions from delegates and discussion by the speakers on the availability of new treatments such as liraglutide thereby promoting the medicine to health professionals prior to the grant of the marketing authorization. Lilly questioned the validity of Novo Nordisk's assertion that only the regional medical advisor remained during the debate; this was contrary to the observations of Lilly staff who also attended this meeting.

Lilly alleged that this activity constituted the pre-licence promotion of liraglutide, it invited misleading claims and comparisons with licensed medicines and constituted the disguised promotion of liraglutide. As such it was in breach of Clause 3.1, 7.2, 7.3 and 12.1. Given the serious nature of the matter Lilly also alleged that this activity was in breach of Clauses 9.1 and 2.

RESPONSE

Novo Nordisk referred to inter-company dialogue in which it submitted that the meeting agenda and contents were organised by the diabetes network entirely independently of Novo Nordisk; the company's only involvement was to pay to the diabetes network to allow it to set up a promotional stand in the meeting room. Novo Nordisk understood that Lilly and Sanofi-Aventis similarly paid to have stands in the meeting room.

Novo Nordisk submitted that one hour of the meeting was dedicated to the debate 'This house believes that GLP-1 agonists (such as exenatide and liraglutide) are the best second line therapy for type 2 diabetes'. This debate was decided upon and organised entirely independently of Novo Nordisk, and it had no involvement in choice of speaker, slide selection or topics for discussion.

The meeting was attended by Novo Nordisk sales representatives and a regional medical advisor. Following lunch, and before the debate, the Novo Nordisk promotional stand was dismantled, and the sales representatives left the meeting room. The regional medical advisor had verbal permission from the meeting organiser to stay in the meeting room for the debate. It was made very clear by both presenters during the debate that liraglutide was unlicensed and that exenatide had been licensed. Due to Novo Nordisk's limited involvement in the organisation of the meeting, and the clear lack of involvement in the debate, the company firmly refuted the allegations that it had breached the Code.

Novo Nordisk submitted that as it had no involvement in choice of speakers, slide selection or topics for discussion it could not provide the slide sets used during the debate. The allegation that the meeting was attended by sales representatives was not correct. Although Novo Nordisk sales representatives were at the venue they left the auditorium before the debate started. The debate was only attended by the local regional medical

advisor from Novo Nordisk. Furthermore any promotional activity on the promotional stand which was located outside the auditorium ceased and the stand was dismantled before the debate started.

Novo Nordisk could not provide a list of attendees because the meeting was organized by local health professionals, not Novo Nordisk.

In response to a request for further information Novo Nordisk stated that the speakers were ultimately chosen by the main organiser of the meeting, who was also responsible for the meeting agenda. Novo Nordisk knew about the agenda and the topics at the beginning of February 2009 when local organisers forwarded it to the company.

PANEL RULING

The Panel was concerned about the arrangements for the meeting. Novo Nordisk knew about the agenda about a month before the meeting. The topic of the debate that agents such as exenatide and liraglutide were the best second line therapy for type 2 diabetes was of concern given that one product had a marketing authorization and the other did not but was about to be so authorized. The title of the debate implied that both products were licensed and this was not so.

The Panel noted that Novo Nordisk had denied the allegation that its sales representatives were present during the debate; Novo Nordisk submitted that only its local regional medical advisor was present. The Panel was concerned, given the title of the debate, that the regional medical advisor had attended even though Novo Nordisk submitted it had a clear lack of involvement in the debate. The Panel had similar concerns to those mentioned in point 4 above. Novo Nordisk stated that the speakers were ultimately chosen by the main organiser of the meeting. There was no evidence before the Panel about the extent to which, if at all, Novo Nordisk had been able to influence or comment upon speaker selection. However Novo Nordisk had no involvement in the slide selection or topics for discussion. The Panel did not consider that Novo Nordisk's payment for an exhibition stand at the meeting meant that Novo Nordisk had sponsored the meeting and was responsible for its content. The Panel noted its concerns about the title of the debate and Novo Nordisk's knowledge thereof. However, on the evidence before it, the Panel decided that Novo Nordisk was not responsible for content of this meeting and thus no breach of Clauses 3.1, 7.2, 7.3 and 12.1 was ruled. The Panel also ruled no breach of Clauses 2 and 9.1.

6 Annual Conference of a diabetes managed clinical network conference, April 2009

This meeting involved the discussion of various diabetes related topics by way of formal presentations and workshops and included a workshop focussing on the incretin mimetics.

COMPLAINT

Lilly alleged that although this meeting was facilitated by Novo Nordisk its sponsorship was not declared on the conference agenda. Novo Nordisk also had a promotional stand at the meeting and in particular, three of its sales representatives together with a sales manager attended the presentations and workshops which discussed incretin mimetics.

Lilly noted that in inter-company correspondence Novo Nordisk acknowledged that it 'helped fund the travel expenses of a visiting professor' and also did not ensure the necessary declaration of this sponsorship in relation to the meeting materials. This was attributed to error and the medical department not being told about the meeting.

Whilst the latter explanation offered no mitigation, Lilly questioned the validity of Novo Nordisk's assertion that the professor was invited by the diabetes managed clinical network independently of Novo Nordisk. Lilly had it on good authority that the professor's input was facilitated by Novo Nordisk and that this included payment of an honorarium. This could be disclosed should it be required.

Lilly alleged that the professor's presentation 'Emerging New therapies in Diabetes Care' involved an unbalanced discussion of Byetta and liraglutide and specifically invited a comparison of the two. In particular, reference was made to unpublished data derived from Novo Nordisk's Lead 6 study which involved a head-to-head comparison of Byetta and liraglutide. There was no clear indication of the licensed status of liraglutide and the impression created, by association to Byetta, was that liraglutide was available and a clinically relevant treatment option in the management of type 2 diabetes.

Lilly was also disappointed that both the speaker and Novo Nordisk disparaged Byetta throughout the presentation by referring to it as 'lizard spit'. Further, the discussion of Byetta was unbalanced and relatively abbreviated compared with the information provided on liraglutide. To compound matters the speaker also conveyed the message that Byetta was only a 50% homologous in comparison to human (physiological) GLP-1; although factually correct, the context in which this was discussed implied an inferior efficacy of Byetta in reducing blood glucose. The speaker also inferred that liraglutide was developed later than Byetta because Novo Nordisk had deliberately taken longer researching this medicine in a more scientific way and hence liraglutide 97% homologous with human GLP-1; the implication being that Lilly had not conducted proper scientific research leading to the development of inferior products such as Byetta.

This presentation and the attendant workshop represented the pre-licence and disguised promotion of liraglutide which was further illustrated by the discussion of data comparing

reduction of HbA_{1c} and weight loss data for Byetta and liraglutide. This was misleading as it implied, by association to Byetta, a licensed product, that liraglutide was also available and clinically relevant.

This activity constituted the pre-licence promotion of liraglutide, it invited misleading claims and comparisons with licensed medicines and constituted the disguised promotion of liraglutide. Lilly alleged breaches of Clauses 3.1, 7.2, 7.3, and 12.1 and, given the serious nature of the matter, a breach of Clauses 9.1 and 2.

Lilly alleged that it was evident that Case AUTH/2202/1/09 did not represent an isolated instance of the pre-licence promotion of liraglutide by Novo Nordisk but was part of a concerted commercially driven objective. The above examples clearly demonstrated that Novo Nordisk had consistently, intentionally and widely promoted the availability of liraglutide in the UK prior to the grant of a marketing authorization. It was also evident that both the medical department and sales department of Novo Nordisk had failed to enforce the necessary standards with regard to compliance with the Code and also, on the company's own admittance, its internal policies and procedures.

Given Novo Nordisk's failure to provide the requested undertakings and in the absence of any compelling or reasonable explanation to the contrary, Lilly alleged that all of the above Novo Nordisk sponsored activity constituted and evidenced the previous and ongoing pre-licence promotion of liraglutide to health professionals and therefore contravened the Code.

In response to a request for further information Lilly stated that the undisclosed information it had regarding the honorarium paid to the professor was obtained from the managed care network which verbally confirmed that it had been paid £800 by Novo Nordisk to cover the professor's honorarium as a speaker. The managed care network then paid the professor.

Further, Lilly alleged that a Novo Nordisk sales representative provided transport to the professor from the airport to the meeting and then onwards to another meeting; this clearly did not reconcile with Novo Nordisk's position that the diabetes managed clinical network selected and invited the speaker entirely independently of the company.

RESPONSE

Novo Nordisk referred to inter-company dialogue in which it submitted that the annual conference of the diabetes managed clinical network was arranged by that organisation itself. Novo Nordisk was asked to help fund the travel expenses of a visiting professor. The diabetes managed clinical network selected and invited the speaker entirely independently of Novo Nordisk. However, Novo Nordisk accepted that it should have declared this funding on the agenda/speaker slides. Novo Nordisk had a clear policy regarding the approval of meetings that it sponsored. Unfortunately, in this particular case it appeared that this had 'slipped through the net' and the medical department was not told of the meeting. Novo Nordisk was looking into the issues leading up to this error and would take steps to ensure that such did not occur again. The sales representatives involved had been reminded in the strongest terms of the importance of not being at or involved in meetings which discussed pre-licence or off-licence data.

In summary, Novo Nordisk prided itself on being a professional, responsible and ethical company, and on ensuring all activities complied with the Code. All staff received training and regular updates and adopted a rigorous approach to ensuring that activities fully complied with the Code.

Finally, Novo Nordisk stated that it had established a new legal and compliance department and one of its tasks was to review compliance procedures. As an initial step, an external consultant would audit the internal compliance procedures and advise as to how Novo Nordisk could confidently improve its processes. The consultant's detailed audit process was provided. This was confidential material. Novo Nordisk asked that the Authority did not reveal this document to Lilly. Novo Nordisk was confident that with the contribution of the new legal and compliance department and the help of its external consultant, it would further improve its internal process to ensure strict compliance with the Code and would help to avoid any future errors.

Furthermore Novo Nordisk submitted that its sales representatives did not have any promotional material concerning liraglutide, since such materials would clearly breach the Code as the product did not have a marketing authorization. A positive opinion from the Committee for Medicinal Products for Human Use for the approval of liraglutide in the treatment of type 2 diabetes was received on 23 April. The marketing authorization was expected to be granted on 29 June 2009.

Novo Nordisk could not provide a delegate list because this meeting was organized by local health professionals without involving Novo Nordisk in the process.

In response to a request for further information Novo Nordisk stated that it had tried, unsuccessfully, to contact the professor several times to clarify the source of the slides which showed unpublished Novo Nordisk data. Novo Nordisk still did not know where these materials came from but guessed that the most likely scenario was that the professor obtained the slides from a global advisory board organised by headquarter colleagues in Copenhagen.

PANEL RULING

The Panel noted that the professor's presentation included background information about GLP-1. A

slide of a Gila Monster lizard was included and another slide headed 'GLP-1 analogues-available/in development' stated that Byetta came from Gila saliva. The next product mentioned on this slide was liraglutide with details that it was once daily. There was no distinction as to which medicines had marketing authorizations and which did not. Similarly a slide headed 'Efficacy of incretin therapeutics' unfavourably compared HbA_{1c} and body weight loss for Byetta with that for liraglutide and included FPG decreases and HbA_{1c} reductions for Januvia (sitagliptin) and Galvus (vildagliptin). The only product that did not have a marketing authorization was liraglutide and again no mention of this difference was made in the slides. Two other slides showed statistically significant advantages for liraglutide over exenatide in reduction of HbA_{1c} and improvement in beta-cell function over 26 weeks. The final slides referred to the pipeline for type 2 diabetes therapy.

The Panel noted there was a discrepancy between the agenda which listed the presentation as 'Emerging New Therapies in Diabetes Care' and the slide presentation which was called 'Emerging drug therapies for diabetes making the alphabet work for T2DM'.

The Panel was extremely concerned about the arrangements for Novo Nordisk's involvement in this meeting. It was not clear from Novo Nordisk's submission whether it had paid travel expenses only or paid an honorarium as alleged by Lilly. The role, if any of a Novo Nordisk representative in providing/facilitating transport to and from the meeting was not clear. The agenda did not refer to Novo Nordisk's sponsorship of the professor. It was unacceptable for this not to be made clear on the documentation (Clause 19.3). In this regard the Panel considered that high standards had not been maintained and a breach of Clause 9.1 was ruled.

The Panel noted Novo Nordisk's submission that the meeting was arranged by the diabetes managed clinical network which had selected and invited the speaker entirely independently of Novo Nordisk. However Novo Nordisk had contributed to the costs of the professor. Companies could not fund or otherwise facilitate a speaker as a means of avoiding the requirements of the Code. Given the title of the professor's presentation 'Emerging New Therapies in Diabetes Care' and the role of Novo Nordisk it should have seen the materials prior to the presentation. The Panel was also concerned that Novo Nordisk was unsure as to where the professor had obtained Novo Nordisk unpublished material. Novo Nordisk should have checked the position with its head office.

Taking all the circumstances into account the Panel considered that, given Novo Nordisk's role, the sponsored presentation in effect promoted an unlicensed medicine. Thus a breach of Clause 3.1 of the Code was ruled. This was disguised promotion and breach of Clause 12.1 was also ruled. The material was misleading and included misleading comparisons. Breaches of Clauses 7.2 and 7.3 were ruled. High standards had not been maintained and a breach of Clause 9.1 was ruled.

The Panel noted that Novo Nordisk had facilitated the professor's attendance and that he had somehow been given access to the company's unpublished data on file. The company's association with the speaker should have been made clear to the delegates. Novo Nordisk's omission in this regard reduced confidence in and brought discredit upon the industry. A breach of Clause 2 was ruled.

* * * * *

The Panel was extremely concerned that Novo Nordisk had promoted a medicine prior to the grant of its marketing authorization on a number of occasions. There appeared, in general, to be a poor understanding of the requirements of the Code. Novo Nordisk had acknowledged that its procedures were lacking; communication at all levels within the company was inadequate. The Panel considered that the circumstances warranted reporting Novo Nordisk to the Code of Practice Appeal Board for it to consider the matter in accordance with Paragraph 8.2 of the Constitution and Procedure.

COMMENTS FROM NOVO NORDISK ON THE REPORT TO THE APPEAL BOARD

Novo Nordisk submitted that its compliance systems and procedures with regard to the Code were currently under extensive review and improvement.

Novo Nordisk stated that staff from its headquarters in Denmark were involved in the materials at issue in points 1 and 2 above (the educational website and the sponsored journal supplement respectively). Novo Nordisk UK understood that any material available to UK health professionals must comply with the Code. To this end it was developing detailed training and retraining programmes relating to relevant parts of the Code for its international colleagues to highlight the need to ensure that global material disseminated to a UK audience was reviewed and approved by Novo Nordisk UK to ensure compliance with the Code. Mandatory training was to be provided to corporate vice presidents in international marketing and medical affairs and international medical advisers whose responsibilities included the development of materials for publication by no later than 30 September.

Novo Nordisk UK's Legal and Compliance Manager was on Novo Nordisk's Global Legal and Compliance Board and the UK Marketing Director was a member of the Global Core Commercialisation Team. Both were completely committed to ensuring that the importance of compliance with the ABPI Code was continuously raised with international colleagues and the need to

ensure robust procedures, at a global level, was enforced to avoid further breaches by international colleagues.

Novo Nordisk submitted that the breaches of the Code in relation to the meetings Points 3 and 6 had further affirmed the need for it to reassess its in-house ABPI Code training programme. An external consultant had audited the company's compliance processes and procedures and highlighted the need to provide further Code training to staff. Novo Nordisk had therefore already put together in conjunction with the consultant an extensive mandatory training programme which it planned to roll out to all relevant staff at the UK office in September.

Novo Nordisk had also put in place a full training day for all diabetes field force (sales managers, diabetes care specialists, health development executives and regional medical advisors, etc) in October 2009. A draft agenda was provided. A representative of the Authority was invited to attend as an observer so that Novo Nordisk could demonstrate how seriously it was trying to improve its processes to ensure Code compliance. Novo Nordisk would welcome feedback in relation to its training programme. Novo Nordisk also noted that two of its senior physicians and a senior medical information officer would attend courses on the Code in September and October.

Novo Nordisk intended that by 8 October 2009, all relevant staff would have undertaken appropriate and relevant training in relation to the Code.

The Legal and Compliance Department had formed a Compliance Review Panel which would review and improve all policies and procedures which needed to comply with the Code. Any new or updated procedures would be rolled out, with appropriate training and validation via the Review Panel and/or Novo Nordisk's electronic training system. Ongoing refresher/updating Code training would take place at each of the field force sales conferences (three times annually) and quarterly for Novo Nordisk's UK marketing and medical staff.

Novo Nordisk hoped that the rigorous review of its global and UK procedures, together with its training programme demonstrated its commitment to address the failings with regard to the Code which had been highlighted by the Panel, and would go some way to ensure, as far as possible, that future breaches of the Code would be avoided.

APPEAL BOARD CONSIDERATION

The Appeal Board was extremely concerned about this case; the promotion of a medicine prior to the grant of its marketing authorization was a serious matter and displayed a poor understanding of the requirements of the Code. As well as being prohibited by the ABPI Code, it was also prohibited by the EFPIA Code on the Promotion of Prescription Only Medicines to, and Interactions with, Health Professionals. Headquarters staff in Denmark should know about the EFPIA Code. According to Novo Nordisk the website had been subjected to regulatory and legal review. The Appeal Board was not convinced that Novo Nordisk fully understood the seriousness of the matter and was especially concerned to note that the company had recently been found in breach of the Code for promoting liraglutide prior to the grant of its marketing authorization (Case AUTH/2202/1/09).

The Appeal Board noted that as a result of the rulings in this case Novo Nordisk had instigated a major review of its compliance systems, procedures and training. Code training of headquarters' staff was soon to be conducted by teleconference although the Appeal Board queried whether this was an effective training medium, given the seriousness of the case. The Appeal Board was very concerned about the apparent lack of influence that Novo Nordisk in the UK had over its headquarters in Denmark regarding compliance of material which came within the scope of the UK Code.

The Appeal Board decided in accordance with Paragraph 11.3 of the Constitution and Procedure to require an audit of Novo Nordisk's procedures in relation to the Code to be carried out by the Authority. The audit should be conducted as soon as possible. The Appeal Board suggested that relevant staff from Denmark should be interviewed as part of that audit. On receipt of the audit report the Appeal Board would consider whether further sanctions, including a report to the ABPI Board of Management, were necessary. In addition the Appeal Board decided that Novo Nordisk should be publicly reprimanded.

APPEAL BOARD FURTHER CONSIDERATION

The Appeal Board noted that it had previously decided that Novo Nordisk should be publicly reprimanded.

The Appeal Board was very concerned that as demonstrated in the audit reports of 2004/05 and the October 2009 audit report, Novo Nordisk clearly lacked processes to ensure compliance with the Code. This must be a priority for all including senior staff who must take more personal responsibility. The company must be able to show that this time it could change and develop attitudes and procedures which gave strong support to compliance.

The Appeal Board noted that Novo Nordisk was due to roll out a number of new standard operating procedures (SOPs) with training on them to commence early in 2010. This timeframe had been extended since the audit. The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure to require a further audit of Novo Nordisk's procedures in relation to the Code to be carried out by the Authority. The audit should be conducted in March 2010 when the Appeal Board expected Novo Nordisk's awareness of the Code and processes including the SOPs to be

much improved and more embedded within the company. The re-audit in this case would take place at the same time as the audit required in Case AUTH/2269/9/09. On receipt of the audit report the Appeal Board would decide if further sanctions were necessary.

Upon receipt of the March 2010 audit report the Appeal Board considered that Novo Nordisk's progress was not sufficiently rapid. It still had serious concerns about the company's approach and attitude to the Code. There were still significant problems with certification. Not all the standard operating procedures (SOPs) had been completed and trained out. This was now due to happen at the May sales conference (other than the SOP for medical and educational goods and services).

Overall, the Appeal Board considered that Novo Nordisk still did not appear to appreciate the seriousness of the situation. The Appeal Board considered requiring Novo Nordisk to submit material for pre-vetting as set out in Paragraph 11.3 of the Constitution and Procedure and/or report the company to the ABPI Board of Management. The Appeal Board decided to require another audit in June/July. On receipt of that audit report the Appeal Board would decide whether further sanctions, such as pre-vetting and/or a report to the ABPI Board, were necessary.

Upon receipt of the July 2010 audit report the Appeal Board was concerned that it had taken some time but considered that significant progress had now been made. This must be maintained. The Appeal Board considered carefully all the options available noting that it had already decided that both cases (Cases AUTH/2234/5/09 and AUTH/2269/9/09) should be the subject of a public reprimand. It decided that no further action was necessary.

Complaint received	**28 May 2009**
Undertaking received	**17 November 2009**
Appeal Board Consideration	**17 September, 11 November 2009, 21 April, 8 September 2010**
Interim case report published	**26 January 2010**
Case completed	**8 September 2010**

CASE AUTH/2269/9/09

DIRECTOR v NOVO NORDISK

Breach of undertaking

The Constitution and Procedure was such that when the Director received information from which it appeared that a company might have contravened the Code the company concerned was requested to provide a complete response to the matters of complaint.

From the information received it appeared that Novo Nordisk had continued to use a supplement to The Times contrary to its undertaking given in Case AUTH/2202/1/09. The matter was taken up by the Director as it was the responsibility of the Authority itself to ensure compliance with undertakings.

The matter had come to light as part of preparation for the consideration of the report in Case AUTH/2234/5/09 by the Code of Practice Appeal Board. It was raised with the Director by an independent member of the Appeal Board but played no part whatsoever in the Appeal Board's consideration of the report in that case.

The detailed response from Novo Nordisk is given below.

The Panel noted Novo Nordisk's submission that there was an error in its response of 20 February to the Panel in Case AUTH/2202/1/09. In response to a request for information about the use of the supplement Novo Nordisk had submitted that in addition to its distribution with The Times on 14 November, eighty copies had been distributed by the clinical research group on World Diabetes Day. No copies had been distributed by the sales and marketing teams and there were no plans for further dissemination.

The Panel was now extremely concerned to note that, in addition to the above, the supplement had been put on to the Novo Nordisk UK website on 4 December 2008. This had not been mentioned previously by Novo Nordisk. This was an extremely serious matter; it was of paramount importance that submissions to the Authority were checked for complete accuracy as the effectiveness of self regulation relied upon the integrity of the information provided by pharmaceutical companies. Novo Nordisk had not provided complete information to the Panel.

The Panel noted that in Case AUTH/2202/1/09 it had considered that Novo Nordisk was responsible for the content of the supplement. Novo Nordisk had full editorial control, owned the copyright and was part of the editorial team.

The article at issue, 'Gut protein drug expected to help improve control' recorded an interview with Novo Nordisk's chief science officer. The Panel considered that the inclusion of this article showed that Novo Nordisk had contributed material about liraglutide and so in that regard had been able to influence the content of the supplement in a manner which favoured its interests.

In his interview, Novo Nordisk's chief science officer stated, *inter alia*, that clinical trials of liraglutide had shown that not only did people maintain better control of their blood glucose levels but that it also helped them to lose weight. The Panel considered that patients would read the article and see liraglutide, with its 'single daily injection' and 'better glucose control' as a possible improvement on their current therapy and thus be encouraged to ask their health professional to prescribe it. In this regard the Panel considered it irrelevant that the product was yet unavailable to prescribe. The Panel further considered that the article promoted liraglutide to the public prior to the grant of a marketing authorization. High standards had not been maintained. Breaches of the Code were ruled. Companies should take particular care when producing materials for the public and in this regard the Panel considered that Novo Nordisk had failed to exercise due diligence and thus brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 had been ruled.

Turning to the case now before it, Case AUTH/2269/9/09, the Panel noted that liraglutide (Victoza) was granted a marketing authorization at the end of June 2009. However as the supplement had been ruled in breach of the Code for encouraging patients to ask their health professional to prescribe liraglutide and for advertising a prescription only medicine to the public, these rulings were still relevant. The Panel noted that following the rulings in Case AUTH/2202/1/09 Novo Nordisk removed the flash banner advertising the supplement from its website on 27 March; however an error resulted in the supplement still being available on the website in September 2009. The form of undertaking for Case AUTH/2202/1/09, signed on 9 March 2009, stated that the last time the supplement was distributed was 14 November 2008. This was not so. Novo Nordisk had instructed the communications department to remove the supplement from its website on 3 March 2009. Novo Nordisk then thought that the supplement had been removed from its website on 27 March.

The Panel noted that Novo Nordisk had failed to provide accurate information about the distribution of the supplement in its response to Case

AUTH/2202/1/09 and had failed to provide accurate information about the last date of use of the supplement in its undertaking. The fact that Novo Nordisk thought the supplement was removed from the website on 27 March was too long given the undertaking was dated 9 March 2009. Such a delay was inexcusable. This was compounded by the fact that the supplement had not been removed successfully and that Novo Nordisk had clearly stated that the supplement was last used on 14 November 2008.

Novo Nordisk had failed to comply with its undertaking and thus the Panel ruled a breach of the Code. The Panel considered that high standards had not been maintained and ruled a breach of the Code. The Panel further considered that by not taking sufficient steps to comply with its undertaking, and providing inaccurate information in that undertaking, Novo Nordisk had brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel was extremely concerned about Novo Nordisk's conduct in relation to the Code; the company had twice provided inaccurate information and had not complied with its undertaking given in Case AUTH/2202/1/09. The Panel decided to report the company to the Code of Practice Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure.

The Appeal Board noted that in its presentation, Novo Nordisk focussed on the three week delay between asking for the supplement to be removed from its website (3 March) and it being removed (27 March) (although it could still be accessed by using the search term liraglutide). In the Appeal Board's view the more serious error was the inaccurate information provided to the Panel about the use of the supplement in its response to the complaint and in its undertaking. Self regulation relied upon full and frank disclosure. With regard to the distribution of the supplement, the Appeal Board noted with concern Novo Nordisk's submission at the consideration of the report, that it did not regard the provision of the supplement via its website as 'distribution' or 'promotion'. Novo Nordisk did not appear to appreciate the utmost seriousness of the situation.

The Appeal Board considered that events at Novo Nordisk regarding the provision of inaccurate information, the delayed withdrawal of the supplement and its continued availability on the website despite the efforts to withdraw it demonstrated poor management practices. The company representatives stated that the standard operating procedure (SOP) for withdrawal of material had not been followed. Responsibility for withdrawal of the supplement had been delegated downwards with an apparent abrogation of responsibility. The undertaking in Case AUTH/2202/1/09 had been signed based on inaccurate information provided by a senior manager. In the Appeal Board's view there appeared to be no inherent sense of personal responsibility for compliance with the Code or a full understanding of what that meant. The Appeal Board considered that responsibility for the company culture in that regard resided with the senior management and was apparently lacking. The Appeal Board also expressed concern about the apparent lack of leadership from the medical department.

The Appeal Board noted Novo Nordisk's apology at the consideration of the report; poor communication within the company had caused some of the problems. A number of new senior managers had been appointed and a compliance team had been formed. The company had initiated a major review of its compliance systems, procedures and training. It had undertaken extensive remedial action and there appeared to be a commitment to improvement. A number of new SOPs would be rolled out in December 2009 with staff training in January 2010. The remaining SOPs would be rolled out in April 2010 with training scheduled for May 2010.

The Appeal Board decided in accordance with Paragraph 11.3 of the Constitution and Procedure to require an audit of Novo Nordisk's procedures in relation to the Code to be carried out by the Authority in March 2010. The Appeal Board would look for reassurance that the audit demonstrated a deeper understanding of the Code and that compliance with it was embedded into the company's culture. The audit required in this case would take place at the same time as the re-audit required in Case AUTH/2234/5/09. On receipt of the audit report the Appeal Board would consider whether further sanctions, including a report to the ABPI Board of Management, were necessary.

The Appeal Board further decided that, given its provision of inaccurate information, Novo Nordisk should be publicly reprimanded.

Upon receipt of the March 2010 audit report the Appeal Board considered that Novo Nordisk's progress was not sufficiently rapid. It still had serious concerns about the company's approach and attitude to the Code. There were still significant problems with certification. Not all the standard operating procedures (SOPs) had been completed and trained out. This was now due to happen at the May sales conference (other than the SOP for medical and educational goods and services).

Overall, the Appeal Board considered that Novo Nordisk still did not appear to appreciate the seriousness of the situation. The Appeal Board considered requiring Novo Nordisk to submit material for pre-vetting as set out in Paragraph 11.3 of the Constitution and Procedure and/or report the company to the ABPI Board of Management. The Appeal Board decided to require another audit in June/July. On receipt of that audit report the Appeal Board would decide whether further

sanctions, such as pre-vetting and/or a report to the ABPI Board, were necessary.

Upon receipt of the July 2010 audit report the Appeal Board was concerned that it had taken some time but considered that significant progress had now been made. This must be maintained. The Appeal Board considered carefully all the options available noting that it had already decided that both cases (Cases AUTH/2234/5/09 and AUTH/2269/9/09) should be the subject of a public reprimand. It decided that no further action was necessary.

COMPLAINT

The Constitution and Procedure was such that when the Director received information from which it appeared that a company might have contravened the Code the company concerned was requested to provide a complete response to the matters of complaint (Paragraph 5.1 of the Constitution and Procedure referred).

From information received it appeared that Novo Nordisk had continued to use a supplement to The Times, contrary to its undertaking given in Case AUTH/2202/1/09. The matter was taken up by the Director as it was the responsibility of the Authority itself to ensure compliance with undertakings. Novo Nordisk was accordingly asked to comment in relation to Clauses 2, 9.1 and 25 of the Code.

The matter had come to light as part of preparation for the consideration of the report in Case AUTH/2234/5/09. It was raised with the Director by an independent member of the Code of Practice Appeal Board but played no part whatsoever in the Appeal Board's consideration of the report in that case.

RESPONSE

Novo Nordisk stated that it seemed the supplement was put onto the company website on 4 December 2008 pursuant to the instructions of a senior manager.

It seemed that there was an error in Novo Nordisk's letter of 20 February 2009 to the PMCPA about Case AUTH/2202/1/09. This letter stated that the supplement was only distributed in The Times, and that the clinical research group distributed 80 copies of it on 14 November 2008 and at that point there were no plans for further dissemination, when in fact it had also been put onto Novo Nordisk's website.

On receipt of the PMCPA ruling on 3 March 2009, the senior manager was instructed to arrange for all copies of the supplement held by Novo Nordisk's external agencies to be destroyed, for the website copy to be deleted and to generally ensure that the supplement was recalled and removed from circulation. Unfortunately due to sickness and holiday absences within the communications department the flash banner advertising the supplement was not removed from the front page of the company's website until 27 March 2009.

As such, Novo Nordisk assumed that the supplement had been successfully removed from circulation on 27 March 2009. The company was therefore surprised and shocked to learn from the PMCPA's letter dated 18 September 2009 that the supplement could still be viewed on Novo Nordisk's website. Immediate action was taken to remedy this situation, and an investigation commenced.

It transpired that although the supplement was removed from the website on 27 March 2009 by deleting the front page flash banner and a copy of the pdf version was deleted via a function on the content manager system 'inactive with attachments', the supplement could still be found in the event of a search. On enquiry with Novo Nordisk's technical IT support function in headquarters, it seemed that the supplement was not permanently removed from the 'back pages' of the website due to it being a pdf document which was manually uploaded to the live server when the page was created.

Novo Nordisk deeply regretted that although the supplement was deleted on 27 March 2009, and the links to it were removed, a technical glitch caused the supplement to re-embed itself into the website on a re-boot, despite being previously deleted. Hence the supplement could still be viewed if 'liraglutide' was used as a search term on the website. Novo Nordisk confirmed that this technical abnormality had been investigated and solved and the supplement could no longer be viewed on the UK website.

* * * * *

Novo Nordisk enquired whether the complaint had been raised by a competitor company. The Director had informed Novo Nordisk that the matter was raised with her by an independent member of the Appeal Board during preparation for the consideration of the report in Case AUTH/2234/5/09. It had played no part whatsoever in the Appeal Board's consideration of that report. Novo Nordisk was invited to submit any further comment. None was received.

PANEL RULING

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

The Panel noted Novo Nordisk's submission that there was an error in its response of 20 February to the Panel in Case AUTH/2202/1/09. In response to a request for information about the use of the supplement Novo Nordisk had submitted that in addition to its distribution with The Times on 14

November, eighty copies had been distributed by the clinical research group on World Diabetes Day. No copies had been distributed by the sales and marketing teams and there were no plans for further dissemination.

The Panel was now extremely concerned to note that, in addition to the above, the supplement was put on to the Novo Nordisk UK website on 4 December 2008; a fact not previously mentioned by Novo Nordisk. The Panel considered that this matter was extremely serious. It was of paramount importance that submissions to the Authority were checked for complete accuracy as the effectiveness of self regulation relied upon the integrity of the information provided by pharmaceutical companies. Novo Nordisk had failed to provide complete information to the Panel.

The Panel noted that in Case AUTH/2202/1/09 it had considered that Novo Nordisk was responsible for the content of the supplement. Novo Nordisk had full editorial control, owned the copyright and was part of the editorial team.

The article at issue, 'Gut protein drug expected to help improve control' recorded an interview with Novo Nordisk's chief science officer. The Panel considered that the inclusion of this article showed that Novo Nordisk had contributed material about liraglutide and so in that regard had been able to influence the content of the supplement in a manner which favoured its interests.

In his interview, Novo Nordisk's chief science officer referred to liraglutide stating that clinical trials of the product had shown that not only did people maintain better control of their blood glucose levels but that it also helped them to lose weight. The article stated that the medicine was currently lodged with the relevant authorities in Europe and the US and, if approved, would be expected to be available from mid 2009. In its consideration of Case AUTH/2202/1/09 the Panel did not accept that the supplement in The Times was an acceptable forum to publish the results of clinical trials as submitted by Novo Nordisk. The Panel considered that patients would read the article and see liraglutide, with its 'single daily injection' and 'better glucose control' as a possible improvement on their current therapy and thus be encouraged to ask their health professional to prescribe it. In this regard the Panel considered it irrelevant that the product was yet unavailable to prescribe. A breach of Clause 22.2 was ruled. The Panel further considered that the article promoted liraglutide to the public. A breach of Clause 22.1 was ruled. Further, the product had, in effect, been promoted prior to the grant of a marketing authorization. A breach of Clause 3.1 was ruled. The Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled. The Panel further considered that companies should take particular care when producing materials for the public. The Panel considered that in this regard Novo Nordisk had failed to exercise due diligence and thus brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 had been ruled.

Turning to the case now before it, Case AUTH/2269/9/09, the Panel noted that liraglutide (Victoza) was granted a marketing authorization at the end of June 2009. However as the supplement had been ruled in breach of the Code for encouraging patients to ask their health professional to prescribe liraglutide and for advertising a prescription only medicine to the public, these rulings were still relevant. The Panel noted that following the rulings in Case AUTH/2202/1/09 Novo Nordisk removed the flash banner advertising the supplement from its website on 27 March however an error resulted in the supplement still being available on the website in September 2009. The form of undertaking for Case AUTH/2202/1/09, signed on 9 March 2009, stated that the last time the supplement was distributed was 14 November 2008. This was not so. Novo Nordisk had instructed the communications department to remove the supplement from its website on 3 March 2009. Novo Nordisk then thought that the supplement had been removed from its website on 27 March.

The Panel noted that Novo Nordisk had failed to provide accurate information about the distribution of the supplement to the Panel in its response to Case AUTH/2202/1/09. The company had failed to provide accurate information about the last date of use of the supplement in its undertaking. The fact that Novo Nordisk thought the supplement was removed from the website on 27 March was too long given the undertaking was dated 9 March 2009. Such a delay was inexcusable. This was compounded by the fact that the supplement had not been removed successfully and that Novo Nordisk had clearly stated that the supplement was last used on 14 November 2008.

Novo Nordisk had failed to comply with its undertaking and thus the Panel ruled a breach of Clause 25. The Panel considered that high standards had not been maintained and ruled a breach of Clause 9.1. The Panel further considered that by not taking sufficient steps to comply with its undertaking, and providing inaccurate information in that undertaking, Novo Nordisk had brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel was extremely concerned about Novo Nordisk's conduct in relation to the Code; the company had twice provided inaccurate information and had not complied with its undertaking given in Case AUTH/2202/1/09. The Panel decided to report the company to the Code of Practice Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure.

APPEAL BOARD CONSIDERATION

The Appeal Board noted that in its presentation, Novo Nordisk focussed on the three week delay

between asking for the supplement to be removed from its website (3 March) and it being removed (27 March) (although it could still be accessed by using the search term liraglutide). In the Appeal Board's view the more serious error was the inaccurate information provided to the Panel about the use of the supplement in its response to the complaint and in its undertaking. Self-regulation relied upon full and frank disclosure. With regard to the distribution of the supplement, the Appeal Board noted with concern Novo Nordisk's submission at the consideration of the report, that it did not regard the provision of the supplement via its website as 'distribution' or 'promotion'. In the Appeal Board's view Novo Nordisk appeared not to appreciate the utmost seriousness of the situation.

The Appeal Board considered that events at Novo Nordisk regarding the provision of inaccurate information, the delayed withdrawal of the supplement and its continued availability on the website despite the efforts to withdraw it demonstrated poor management practices. The company representatives stated that the standard operating procedure (SOP) for withdrawal of material had not been followed. Responsibility for withdrawal of the supplement had been delegated downwards with an apparent abrogation of responsibility. The undertaking in Case AUTH/2202/1/09 had been signed based on inaccurate information provided by a senior manager. In the Appeal Board's view there appeared to be no inherent sense of personal responsibility for compliance with the Code or a full understanding of what that meant. The Appeal Board considered that responsibility for the company culture in that regard resided with the senior management and was apparently lacking. The Appeal Board also expressed concern about the apparent lack of leadership from the medical department.

The Appeal Board noted Novo Nordisk's apology at the consideration of the report; poor communication within the company had caused some of the problems. A number of new senior managers had been appointed and a compliance team had been formed. The company had initiated a major review of its compliance systems, procedures and training. It had undertaken extensive remedial action and there appeared to be a commitment to improvement. A number of new SOPs would be rolled out in December 2009 with staff training in January 2010. The remaining SOPs would be rolled out in April 2010 with training scheduled for May 2010.

The Appeal Board decided in accordance with Paragraph 11.3 of the Constitution and Procedure to require an audit of Novo Nordisk's procedures in relation to the Code to be carried out by the Authority in March 2010. The Appeal Board would look for reassurance that the audit demonstrated a deeper understanding of the Code and that compliance with it was embedded into the company's culture. The audit required in this case would take place at the same time as the re audit required in Case AUTH/2234/5/09. On receipt of the audit report the Appeal Board would consider whether further sanctions, including a report to the ABPI Board of Management, were necessary.

The Appeal Board further decided that, given its provision of inaccurate information, Novo Nordisk should be publicly reprimanded.

FURTHER APPEAL BOARD CONSIDERATION

Upon receipt of the March 2010 audit report the Appeal Board considered that Novo Nordisk's progress was not sufficiently rapid. It still had serious concerns about the company's approach and attitude to the Code. There were still significant problems with certification. Not all the standard operating procedures (SOPs) had been completed and trained out. This was now due to happen at the May sales conference (other than the SOP for medical and educational goods and services).

Overall, the Appeal Board considered that Novo Nordisk still did not appear to appreciate the seriousness of the situation. The Appeal Board considered requiring Novo Nordisk to submit material for pre-vetting as set out in Paragraph 11.3 of the Constitution and Procedure and/or report the company to the ABPI Board of Management. The Appeal Board decided to require another audit in June/July. On receipt of that audit report the Appeal Board would decide whether further sanctions, such as pre-vetting and/or a report to the ABPI Board were necessary.

Upon receipt of the July 2010 audit report the Appeal Board was concerned that it had taken some time but considered that significant progress had now been made. This must be maintained. The Appeal Board considered carefully all the options available noting that it had already decided that both cases (Cases AUTH/2234/5/09 and AUTH/2269/9/09) should be the subject of a public reprimand. It decided that no further action was necessary.

Proceedings commenced	**18 September 2009**
Undertaking received	**5 November 2009**
Appeal Board consideration	**11 November 2009, 21 April, 8 September 2010**
Interim case report published	**26 January 2010**
Case completed	**8 September 2010**

CASE AUTH/2308/4/10

MEDIA/DIRECTOR v NORGINE

Lack of sponsorship declaration in published letter

On 20 March, the BMJ published an article entitled 'Generic drugs: protest group was not quite what it seemed'. In accordance with the Authority's Constitution and Procedure, the matter was taken up with Norgine as a complaint by the Director.

The article was about an alleged lack of transparency with regard to Norgine's role in the publication of a letter in The Times (24 February). The letter was headed 'Patient wellbeing at risk from substituted generic medicines'. The article claimed that the letter, which had been signed by several doctors and representatives of patient groups, decried generics and pleaded for doctors' choice to prescribe branded drugs to be paramount. The letter was written in response to the Department of Health's (DoH's) consultation on prescribing which proposed automatic generic substitution. The article claimed that Norgine considered that it would be under direct threat as a result of increased use of generics.

The author of the article in the BMJ stated that far from being a spontaneous protest from a group of patients and health professionals, the letter to The Times had been coordinated by a public relations (PR) agency on behalf of Norgine. The article alleged that the agency had searched the published literature for articles written in support of prescribing branded medicines and then invited the authors of those articles to sign a letter protesting against generic substitution. The article stated, however, that the chief operating officer of Norgine did not add his name to the list of signatories. There seemed to be a lack of transparency.

The author further noted that the letter in The Times had been signed on behalf of three patient organisations which received funding from various pharmaceutical companies and some of the doctors who had signed the letter also advised pharmaceutical companies or received research funding from them.

The detailed response from Norgine is given below.

The Panel first had to decide whether or not the matter was subject to the Code. The Code applied to the promotion of medicines to health professionals and to appropriate administrative staff. The Code also applied to certain areas that were non-promotional, including the provision of information to the public about prescription only medicines. The Code defined promotion and stated that the term promotion did not include information relating to human health or diseases provided there was no reference either direct or indirect, to specific medicines.

The Panel noted that the letter in question referred to prescribed medicines, it focussed on differences between branded and generic medicines and the possible adverse effects on patient wellbeing if pharmacists could automatically substitute a generic medicine even if the doctor had written a prescription for a specific brand. The letter was signed by senior figures from several patient organisations, individual health professionals and others including a previous Director General of the ABPI. No medicine was mentioned by name or unique identifying feature. The Panel noted that it might be argued that the removal of automatic generic substitution would benefit companies by increasing/maintaining the use of branded products ie it would promote the prescription, supply, sale or administration of their medicines. However, given the intended audience, the public, and the content of the letter in question, the Panel decided that the letter to The Times was not 'promotion' as defined in the Code. The letter referred a number of times to prescribing and although not explicitly solely about prescription only medicines such medicines would be covered by the letter. Thus, although not promotional, the Panel considered that the letter was subject to the Code as it was information about prescription only medicines aimed at the public.

The Panel noted that the Code required that material relating to medicines and their uses, whether promotional in nature or not, which was sponsored by a pharmaceutical company must clearly indicate that it had been sponsored by that company. The supplementary information required a declaration to reflect the nature of the company's involvement. The Code did not specifically mention lobbying activities but in the Panel's view if such activities resulted in materials relating to medicines and their uses then the Code applied. In the Panel's view the letter to The Times in contrasting branded and generic medicines clearly referred to medicines and their uses. Norgine's role in the development and production of the letter meant that it was responsible for it under the Code and that Norgine had sponsored the letter. The Code required transparency about pharmaceutical company activities so that readers of the material were aware of such involvement.

The Panel noted Norgine's submission that all of the signatories to the letter knew about Norgine's role in the development and production of the letter. In the Panel's view it was equally important that those reading the published letter were also aware of Norgine's role. There was no mention of Norgine either in the published letter itself or as a signatory to the letter. Nor was there any indication of any pharmaceutical company involvement. In the

Panel's view the majority of those reading the letter in The Times would have viewed it differently if they had known that it had been sponsored by a pharmaceutical company with an interest in the views expressed. The Panel considered that by not making its role clear Norgine had failed to comply with the Code and a breach was ruled. The Panel considered that Norgine had therefore failed to maintain high standards and a further breach was ruled.

The Panel noted that every case had to be considered on its own merits. The Code covered pharmaceutical company relationships with patient organisations and applied to patient organisations and the like when such activities were supported by pharmaceutical companies. In this case the campaign in question was initiated and funded by Norgine. The suggestion that a letter be written to The Times, signed by clinicians and patient group representatives, had come from a company-organised roundtable meeting of key journalists to gather their views on how awareness of the issues involved could be raised amongst the general public. Potential signatories to the letter were identified by Norgine or its PR agency; some had been previously identified to sign a consensus document whilst others were contacted only to sign the letter. The Panel noted that where the letter was signed by individuals from patient organisations the organisation was also named and the signatory's position within the organisation stated ie Chair, President, etc. Individuals with no stated involvement with patient organisations had also signed the letter. The Panel queried whether the letter was developed and produced as a result of a formal interaction between Norgine and the patient organisations or as a more personal interaction with individuals operating wholly independently from their patient organisation. However, as patient organisations were named, and the senior position of each signatory within the organisation given, there was an implication that each organisation formally endorsed the letter. This would certainly be the impression given to readers. Readers would not know from the published letter that a pharmaceutical company was also involved. The Panel considered that Norgine had not made its involvement with the patient organisations named in the letter clear. The Panel ruled a breach of the Code. The Code required wording to accurately reflect the nature of a pharmaceutical company's involvement in the declaration of sponsorship and, in the context of relationships with patient organisations, covered all material sponsored by a pharmaceutical company. Norgine's role in the development and production of the published letter was not clear and a breach of the Code was ruled.

Upon appeal by Norgine, the Appeal Board noted that the letter in question referred to prescribed medicines, it focussed on differences between branded and generic medicines and what might happen to patients if pharmacists could automatically substitute a generic medicine even if a specific brand had been prescribed. No medicine was mentioned by name or unique identifying feature. The letter referred a number of times to prescribing and although not explicitly solely about prescription only medicines such medicines would be covered by the letter. Thus, the Appeal Board considered that the letter was subject to the Code as it was information about prescription only medicines aimed at the public.

The letter to The Times, in contrasting branded and generic medicines, clearly referred to medicines and their uses. The letter had been written as a direct result of a campaign orchestrated by Norgine. Norgine had underwritten the costs of the letter being written. The Code required transparency about pharmaceutical company activities so that readers of the material were aware of any such involvement. The letter itself did not refer to Norgine's involvement and no one from Norgine had signed the letter. In the Appeal Board's view those reading the letter in The Times should have been able to do so in the knowledge that a pharmaceutical company with a vested interest had been involved in its creation. Disclosure in this regard would have allowed the reader to form his own fully informed opinion of the views expressed. The Appeal Board considered that by not making its role clear Norgine had failed to comply with the Code and it upheld the Panel's ruling of a breach.

The campaign in question was initiated and funded by Norgine. The suggestion that a letter be written to The Times, signed by clinicians and patient organisation representatives, had come from a company-organised roundtable meeting of key journalists to gather their views on how awareness of the issues involved could be raised amongst the general public. Potential signatories to the letter were identified by Norgine or its PR agency; some had been previously identified to sign a consensus document whilst others were contacted only to sign the letter. The Appeal Board noted from Norgine's representatives at the appeal that each signatory chose which title to use when signing the letter; some chose to refer to their role in a named patient organisation ie Chair, President, etc. Individuals with no stated involvement with patient organisations had also signed the letter. The Appeal Board considered that as patient organisations were named, and the senior position of each signatory within the organisation given, readers would assume that each organisation formally endorsed the letter. The Appeal Board considered that in any event, by deliberately not providing any indication of its involvement with the production of the letter, Norgine had not made its involvement with the patient organisations noted in the letter clear to those reading it. The Appeal Board upheld the Panel's ruling of a breach of the Code.
The Appeal Board considered that the Code required wording to accurately reflect the nature of a pharmaceutical company's involvement in the declaration of sponsorship from the outset. Norgine's role in the development and production of the letter was not made clear to readers of The Times. The Appeal Board upheld the Panel's ruling

of a breach of the Code.

The Appeal Board noted that the letter was directed at the public and thus it was important that the public were fully informed as to who was behind it; Norgine, by not declaring its involvement in the creation of the letter had therefore failed to maintain high standards and the Appeal Board upheld the Panel's ruling of a breach of the Code.

On 20 March, the BMJ published an article entitled 'Generic drugs: protest group was not quite what it seemed'. The author alleged that an apparently spontaneous letter of protest from patients' groups and health professionals which was published in The Times (24 February) was coordinated by a public relations (PR) company, on behalf of Norgine Pharmaceuticals Limited.

In accordance with Paragraph 6.1 of the Authority's Constitution and Procedure, the matter was taken up with Norgine as a complaint by the Director. The author was asked whether she wished to be involved in the case and whether she had any additional information to submit. The author did not submit any more data but asked to be kept informed.

COMPLAINT

The article was about an alleged lack of transparency with regard to Norgine's role in the publication of the letter in The Times. The letter was headed 'Patient wellbeing at risk from substituted generic medicines'. The article claimed that the letter, which had been signed by several doctors and representatives of patient groups, decried generics and pleaded for doctors' choice to prescribe branded drugs to be paramount. The letter was written in response to the Department of Health's (DoH's) consultation on prescribing which proposed automatic generic substitution.

The article stated that far from being a spontaneous protest from a group of patients and health professionals, the letter to The Times had been coordinated by a public relations agency on behalf of Norgine. The article alleged that the agency had searched the published literature for articles written in support of prescribing branded medicines and then invited the authors of those articles to sign a letter protesting against generic substitution. The article stated, however, that the chief operating officer of Norgine did not add his name to the list of signatories. There seemed to be a lack of transparency.

The author of the BMJ article noted that Norgine had organised a paper to be written by its public relations agency last year in response to the DoH's proposals on prescribing. It was this document which was used initially to gather support. The article claimed that Norgine considered that it would be under direct threat as a result of increased use of generics.

The article in the BMJ noted some of the differences in formulation/presentation of branded medicines and generics and stated that while it was important that patients were happy with their medicines it questioned how much the pharmaceutical industry was allowed to press for non-generics. The author noted that the letter in The Times had been signed on behalf of three patient organisations which received funding from various pharmaceutical companies and some of the doctors who had signed the letter also advised pharmaceutical companies or received research funding from them.

When writing to Norgine the Authority asked it to respond in relation to Clauses 9.1, 9.10, 23.2 and 23.8 of the Code.

RESPONSE

Norgine stated that the letter to The Times arose from a campaign to oppose the introduction of generic substitution in primary care in the UK. The campaign was coordinated by its PR agency and funded by Norgine. This project was initiated in March 2009 and involved a public relations and medical communication campaign to raise awareness amongst health professionals, patients and patient groups as to the possible negative implications for all stakeholders arising from the proposals for automatic generic substitution which had arisen from the latest agreement of the Pharmaceutical Price Regulation Scheme (PPRS).

One of the first activities of this campaign was for Norgine and the PR agency to research the clinical issues surrounding generic substitution, particularly looking at what evidence existed relating to the patient level impact that might occur should generic substitution result in branded medicines being substituted for generic versions.

The next step in the campaign was that the agency produced a draft consensus document entitled 'Automatic Generic Substitution – Clinical implications for patients', which involved further research. This sponsorship by Norgine for the production of this document was clearly declared in the document from first draft stage onwards.

A number of individuals who might have an interest in putting their names to the consensus document were identified jointly between Norgine and the agency, and these individuals were contacted by telephone by the agency. The agency's policy was that in any telephone contact with respect to such a campaign, it was always made clear that the campaign was being conducted on behalf of a sponsor company, which was always specifically named.

As part of the campaign, the agency proposed that an advisory board in the form of a consumer roundtable meeting be held to which were invited leading medical correspondents from the lay press. A number of medical correspondents attended this meeting, and the idea of a letter to The Times was

proposed at this meeting by the journalists themselves.

Following the meeting, Norgine agreed to cover the agency's costs for producing this letter as part of the ongoing campaign.

The agency wrote and sent the first draft of the letter to the signatories, a number of whom made revisions to the first draft. These revisions were incorporated in the final draft, which was sent to the signatories for approval, and the letter was then sent to The Times by one of the signatories on behalf of the others.

The letter was published in The Times newspaper on 24 February 2010 and contained the names of nine of the signatories of the letter. The full list of nineteen signatories appeared in the timesonline web site.

Potential signatories first approached were those individuals who had already signed the consensus document 'Automatic Generic Substitution – Clinical implications for patients'. These signatories were approached by the agency and asked if they were prepared to put their names to a letter to The Times.

Other potential signatories were suggested both by Norgine and the agency and these additional signatories were also telephoned by the agency, when Norgine's involvement was disclosed as per the agency's policy as above.

The agency coordinated the project with oversight and direction from Norgine as described in the contract.

No honoraria or payments or benefits in kind of any description were made to the signatories of the letter, either directly or indirectly.

The letter was not certified under the Code. The letter was the result of discussions and opinions of those involved who freely became signatories. As the letter was not within the scope of the Code, certification was not required.

Before focusing upon the specific clauses of the Code which it had been requested to address, Norgine maintained that the publication of the letter to The Times which was the basis of the complaint, including all of the related interactions, was not within the scope of the Code. Norgine however recognised the importance of transparency and its continued support of both the letter and the spirit of the Code. Thus, in the interests of facilitating the prompt resolution of this matter, and without prejudice, it had provided the information requested. Norgine stated that all its dealings were conducted in a professional and transparent manner, consistent with the Code and Norgine's ethical principles.

With regard to Clause 9.10, Norgine submitted that the letter in The Times was outside the scope of the Code and did not constitute a breach of this clause.

The letter and the allied activities described above were outside the scope of the Code as described in Clauses 1.1 and 1.2. This was not a promotional activity and no specific medicine or groups of medicines had been referred to, other than a range of examples from various therapeutic areas directed at demonstrating the potential impact of generic substitution.

The closest reference to this type of activity within Clause 1 was the exclusion contained within Clause 1.2 which stated that promotion did not include 'information relating to human health or diseases provided there is no reference, either direct or indirect, to specific medicines'.

As described above, the letter arose from the consensus document 'Automatic Generic Substitution – Clinical implications for patients', the preparation of which was sponsored by Norgine. This sponsorship was clearly declared in that document. All parties involved would have been made aware of Norgine's role.

The letter in The Times was about proposed changes to the arrangements for the prescription and dispensing of medicines in the UK. It arose as part of a political lobbying campaign and as such could not be considered as material specifically related to a specific medicine or medicines and their uses, which was the normal interpretation of Clause 9.10. The type of material usually covered under this clause were sponsored journal supplements and the like which referred to specific medicines or diseases.

Clause 9.10 did not cover, and there was no precedent for the use of this clause to cover, political lobbying campaigns undertaken by the pharmaceutical industry.

Norgine recognised that companies had a responsibility to ensure that any such material was factually accurate and not misleading. Given that the Code was not constituted to regulate pharmaceutical companies' political lobbying campaigns which were unrelated to any particular medicine or medicines, for the reasons above Norgine did not believe that these activities and the letter specifically were within the scope of the Code. Any material produced as part of such a non product-related lobbying campaign must therefore be outside the scope of Clause 9.10 of the Code, and therefore it refuted any allegation of a possible breach of Clause 9.10.

Norgine submitted that with regard to Clause 23.2 irrespective of the fact that its lobbying activities, and the letter itself were outside the scope of the Code, Norgine was very aware that particular care needed to be taken in any interaction with patient organisations and individuals representing such organisations. Norgine stated that, since its relationship was not in support of their work and no financial or other 'in kind' sponsorship occurred, Norgine's activities did not come within the scope of Clause 23. Nonetheless, Norgine acted in

accordance with the spirit of the Code, ensuring that its involvement in the lobbying activities was clear from the initial contact and throughout the period.

Therefore in this campaign, the PR agency acting on behalf of Norgine and consistent with its own written ethical policies, made sure that Norgine's involvement was transparent and made clear from the very first contact.

The agency's relationship with the patient organisations was two fold. Firstly supplying them with background information to enable the patient organisations to respond to the generic substitution proposals and the subsequent DoH public consultation, and secondly to see which patient organisations would support and put their name to the consensus document.

A number of individuals and patient organisations who might have an interest in putting their names to the consensus document were identified jointly by Norgine and the agency, and the agency contacted these individuals and individuals representing patient organisations by telephone. It was important to note that it was the policy of the agency that in any telephone contact made to an individual with respect to such a campaign, it was made clear that the campaign was being conducted on behalf of a sponsor company, which was always specifically named.

The information provided by Norgine and/or the agency was not product or medicines related and had been reviewed internally by Norgine to ensure that this was so.

Notwithstanding its contention that these activities did not come within the purview of the Code, Norgine nonetheless submitted that its involvement was made clear, and therefore, in any event, there was no breach of Clause 23.2.

With regard to Clause 23.8 all representatives of patient organisations who were contacted were told about Norgine's involvement from the outset as stated above both in the initial communication by the agency and in the consensus document itself. As a lobbying initiative unrelated to particular medicines or groups of medicines this activity was outside the scope of the Code. It was however important to recognise that neither Norgine nor the agency sponsored any of the patient organisations or signatories to the letter.

The declaration of Norgine's involvement in the consensus document stated: 'The document was researched using interviews with healthcare providers, patient associations and published literature, and drafted by a medical writer [named] funded by Norgine'. Norgine submitted that this declaration accurately reflected the nature of Norgine's involvement as required by Clause 23.8.

Norgine therefore submitted that given that there was no sponsorship of any signatories to the letter and the involvement of Norgine was made clear and acknowledged from the outset, were the Code to apply, which it contended was not the case, there was no breach of Clause 23.8.

With regard to Clause 9.1 Norgine reiterated its assertion that this activity was outside the scope of the Code, but nevertheless and without prejudice, maintained that both Norgine and the agency, had consistently maintained the highest standards with respect to this whole campaign and in particular the circumstances which led up to the letter in question being published in The Times. Norgine's compliance procedures were rigorously applied, and as described above, Norgine ensured that a responsible level of internal review was conducted even in circumstances where such scrutiny was not required. As such it refuted any breach of Clause 9.1.

In summary Norgine stated that it was outside the scope of the Code to regulate how pharmaceutical companies worked with medical communications and public relations companies in political lobbying campaigns which were completely unrelated to any particular medicine or medicines. In particular any material produced as part of a non product-related lobbying campaign was outside the scope of Clause 9.10. This 'material' in the broadest sense might include letters to the lay press.

When these sorts of activities involved contact with patient organisations, either directly by a pharmaceutical company or by a medical communications company working on behalf of a pharmaceutical company, then Norgine recognised that working with patient organisations needed to comply with the requirements of Clause 23 of the Code, if applicable. In all circumstances, whether or not Norgine's contact with the patient organisation was within the scope of the Code, Norgine as a matter of principle and policy ensured that this relationship was conducted in a transparent, professional and ethical manner.

The signatories to the letter were all individuals of the highest probity, who were made fully aware of Norgine's involvement in this campaign and the letter. No sponsorship of any of the signatories to the letter occurred, and all signatories signed the letter of their own free will.

Norgine believed that the evidence demonstrated that in the interactions between the PR agency and patient organisations the involvement of Norgine was fully transparent and made clear from the outset, and that Norgine had demonstrated that there was no sponsorship to the signatories. Therefore if the Code were to apply, which it contended was not the case, there would in such event be no breach of either Clause 23.2 or Clause 23.8.

Norgine stated that it responded to this complaint as a matter of process and its willingness to comply with the Code, but strongly restated its contention that this was not a matter for the Code and was

therefore outside the jurisdiction of the PMCPA.

In the event that the PMCPA concluded that this matter was within the scope of the Code and that further enquiry was necessary, Norgine challenged the ability of PMCPA normal procedures to address the resolution of this complaint because of a conflict of interest. The topic of this complaint, ie the negative implications of the proposals for generic substitution, was one in which the ABPI had a vested interest given its support for this proposal. The contrary views of Norgine and the ABPI on the subject of generic substitution were well known, and the participation of ABPI employees on the Panel would be prejudicial to Norgine's right to a fair hearing on the determination of whether there had been a breach of the Code.

PANEL RULING

The Panel noted Norgine's comments about a potential conflict of interest. The PMCPA operated independently of the ABPI itself. The Director of the Authority was employed by the ABPI but reported to the Appeal Board in relation to all matters concerning the interpretation of the Code and its operation, and to the President of the ABPI solely for administrative purposes. This was made clear in Paragraph 1.3 of the Constitution and Procedure. There was no reporting line to the Director General of the ABPI. No PMCPA staff, including the Panel, was in any way concerned or involved with ABPI policy on any subject other than matters relating in general to the Code and its operation. The Panel's role was to consider the matter in relation to the Code bearing in mind the material provided by the parties and in accordance with the Constitution and Procedure.

The first decision was whether or not the matter was subject to the Code. Clause 1.1 made it clear that the Code applied to the promotion of medicines to health professionals and to appropriate administrative staff. The Code also applied to certain areas that were non-promotional, including the provision of information to the public about prescription only medicines. Clause 1.2 of the Code defined promotion and that the term promotion did not include information relating to human health or diseases provided there was no reference either direct or indirect, to specific medicines.

The Panel noted that the letter in question referred to prescribed medicines, it focused on differences between branded and generic medicines and the possible adverse effects on patient wellbeing if pharmacists could automatically substitute a generic medicine even if the doctor had written a prescription for a specific brand. The letter was signed by senior figures from several patient organisations, individual health professionals and others including a previous Director General of the ABPI. No medicine was mentioned by name or unique identifying feature. The Panel noted that it might be argued that the removal of automatic generic substitution would benefit companies by increasing/maintaining the use of branded products ie it would promote the prescription, supply, sale or administration of their medicines. However, given the intended audience, the public, and the content of the letter in question, the Panel decided that the letter to The Times was not 'promotion' as defined in Clause 1.2 of the Code. The letter referred a number of times to prescribing and although not explicitly solely about prescription only medicines such medicines would be covered by the letter. Thus, although not promotional, the Panel considered that the letter was subject to the Code as it was information about prescription only medicines aimed at the public.

The Panel noted that Clause 9.10 required that material relating to medicines and their uses, whether promotional in nature or not, which was sponsored by a pharmaceutical company must clearly indicate that it had been sponsored by that company. The supplementary information required a declaration to reflect the nature of the company's involvement. Clause 9.10 did not specifically mention lobbying activities but in the Panel's view if such activities resulted in materials relating to medicines and their uses then Clause 9.10 applied. In the Panel's view the letter to The Times in contrasting branded and generic medicines clearly referred to medicines and their uses. Norgine's role in the development and production of the letter meant that it was responsible for it under the Code and that Norgine had sponsored the letter. The purpose of Clause 9.10 was to require transparency about pharmaceutical company activities so that readers of the material were aware of such involvement.

The Panel noted Norgine's submission that all of the signatories to the letter knew about Norgine's role in the development and production of the letter. In the Panel's view it was equally important that those reading the published letter were also aware of Norgine's role. There was no mention of Norgine either in the published letter itself or as a signatory to the letter. Nor was there any indication of any pharmaceutical company involvement. In the Panel's view the majority of those reading the letter in The Times would have viewed it differently if they had known that it had been sponsored by a pharmaceutical company with an interest in the views expressed. The Panel considered that by not making its role clear Norgine had failed to comply with Clause 9.10. A breach of that clause was ruled. The Panel considered that Norgine had therefore failed to maintain high standards and a breach of Clause 9.1 was also ruled.

The Panel noted that every case had to be considered on its own merits. Clause 23 of the Code covered pharmaceutical company relationships with patient organisations and applied to patient organisations and the like when such activities were supported by pharmaceutical companies. In this case the campaign in question was initiated and funded by Norgine. The suggestion that a letter be written to The Times, signed by clinicians and

patient group representatives, had come from a company-organised roundtable meeting of key journalists to gather their views on how awareness of the issues involved could be raised amongst the general public. Potential signatories to the letter were identified by Norgine or its agency; some had been previously identified to sign a consensus document whilst others were contacted only to sign the letter. The Panel noted that where the letter was signed by individuals from patient organisations the organisation was also named and the signatory's position within the organisation stated ie Chair, President, etc. Individuals with no stated involvement with patient organisations had also signed the letter. The Panel queried whether the letter was developed and produced as a result of a formal interaction between Norgine and the patient organisations or as a more personal interaction with individuals operating wholly independently from their patient organisation. However, as patient organisations were named, and the senior position of each signatory within the organisation given, there was an implication that each organisation formally endorsed the letter. This would certainly be the impression given to readers. Readers would not know from the published letter that a pharmaceutical company was also involved. The Panel considered that Norgine had not made its involvement with the patient organisations named in the letter clear. The Panel ruled a breach of Clause 23.2. Clause 23.8, like Clause 9.10, required wording to accurately reflect the nature of a pharmaceutical company's involvement in the declaration of sponsorship but was not similarly limited to material about medicines and their uses but, in the context of relationships with patient organisations, covered all material sponsored by a pharmaceutical company. Norgine's role in the development and production of the published letter was not clear. A breach of Clause 23.8 was ruled.

APPEAL BY NORGINE

Norgine explained that the background to this complaint was the perceived benefits and potential risks of generic substitution and a potential change in UK health policy on this issue. Compulsory or automatic generic substitution was the practice by which a pharmacist would dispense a generic version of a medicine despite the fact that the prescriber had prescribed the medicine by brand name.

Generic substitution was proposed by the ABPI at the last renegotiation of the PPRS. This proposal was initially rejected by the DoH, but later accepted. The alternative proposal from the DoH to reduce expenditure on medicines in 2010 was an across the board price cut for all medicines that would, unlike the generic substitution proposal, affect all member companies roughly in equal measure. The ABPI's proposal was in direct conflict with ABPI policy at the time.

Norgine submitted that differing views on the implications of generic substitution (which could come in many forms) were honestly held by various interested parties, but it was without doubt an important matter of health policy and principle that was not directly concerned with specific medicines and their uses. It needed careful consideration because in some cases it had the potential to have a serious negative impact on patient wellbeing.

Norgine submitted that it had, therefore, in the consultation being conducted by the DoH, taken an entirely different position to the ABPI and its members. As this complaint originated from the PMCPA itself and concerned Norgine's lobbying against the ABPI's interests on the generic substitution proposals, the ABPI and its member companies and affiliated organisations had a potential conflict of interest that undermined their ability to be seen to act without bias. As with all conflicts of interest this applied regardless of whether there was evidence of bias. This issue, therefore, affected the Panel's role in relation to its initial decision to deal with the article in the BMJ as a complaint and in relation to its initial ruling, and affected the appeal being heard by any members of the Appeal Board who were employees of ABPI member companies.

As a preliminary point, therefore, Norgine sought a determination by the Chairman of the Appeal Board on the issue of conflict of interest and how the Appeal Board might be constituted to avoid any perception of possible bias.

Grounds for appeal

Norgine submitted that the core of its appeal was that the Panel was incorrect to conclude that the letter fell within the scope of Clause 1.1. The focus of the Code was the promotion of medicines. However, it also covered certain non-promotional activities. Norgine noted that non-promotional materials were treated as outside the European Federation of Pharmaceutical Industries and Associations (EFPIA) Code of Practice and whilst that code encouraged member associations to consider where it might be appropriate to have provisions relating to non-promotional information, Norgine submitted that exceptions to the general rule that the Code was about promotion of medicines should be clearly stated and restrictively construed.

Norgine submitted that the relevant paragraph of Clause 1.1 stated 'The Code also applies to a number of areas which are non-promotional, including information made available to the public about prescription only medicines'.

Norgine submitted that because 'information' was not defined in the Code, the term should be given its natural meaning. A typical thesaurus entry for 'information' gave the following synonyms: info, data, statistics, facts, figures, gen, material, evidence. It was helpful in understanding the intended meaning of 'information' in respect to Clause 1.1 if one or two synonyms were substituted, for example: 'The Code also applies to … data made

available to the public about prescription only medicines,' or 'The Code also applies to … facts made available to the public about prescription only medicines.'

Norgine submitted that this exercise clarified the intention of Clause 1.1, which was, quite reasonably, to bring into the scope of the Code the provision to the public of information, data or facts about prescription only medicines. On this basis it was completely appropriate, for instance, that press releases about particular medicines, and the progress made in research of their uses or their authorization and launch should be covered by the Code. In contrast it was inappropriate to stretch the Code to cover this type of lobbying activity on health policy.

Norgine submitted that examined from this perspective, the letter to The Times had nothing to do with the provision of information, data or facts about any prescription medicine or medicines. Health policy in this industry necessarily referred to medicines as the background field of activity, but health policy in relation to pricing or generic substitution and similar topics transcended issues and facts concerning particular medicines or their uses or health information that discussed treatment options for particular conditions. Therefore, the current debate concerned itself solely with the proposed changes to the way in which prescribed medicines were dispensed. Whilst prescribing was mentioned in the letter, the explicit references to prescribing did not provide any information (data or facts) about medicines. These references merely highlighted the fact that the prescribing decision could be impacted by separate decisions upon dispensing that might have an unintended impact upon the patient.

Norgine suggested that indirect references to medicines in this way were not intended to be covered by Clause 1.1 and should be deemed to be outside the scope of the Code.

Norgine submitted that such legitimate comment by interested parties about general issues of health policy, unconnected with specific medicines, groups of medicines or disease awareness, was not, and should not, be regulated by the Code. The letter in question referred to none of these areas and as such it was outside the scope of the Code.

Clause 9.10

Regarding the alleged breach of Clause 9.10, consistent with its argument above, Norgine submitted that the letter at issue was outside the scope of the Code and did not constitute a breach of this clause. Clause 9.10 only related to 'material relating to medicines and their uses' (whether promotional or not). A restriction of the scope of Clause 9.10 to 'medicines and their uses' was consistent with the limited extension of the Code, as described in Clause 1.1, to matters such as 'information made available to the public about prescription only medicines'. The letter in The Times was about proposed changes to the arrangements for the prescription and dispensing of medicines in the UK. It arose out of a political lobbying campaign and as such could not be considered as material specifically related to a specific medicine or medicines and their uses, which was the concern of Clause 9.10.

Norgine submitted that lobbying activities must be treated as outside the Code unless they related to specific medicines. It was a potentially dangerous extension of the Code to conclude that lobbying activities, which resulted in materials relating to dispensing principles or other health policy issues, came within the scope of Clause 9.10. The letter was not about the use of medicines, but dispensing principles. There was no precedent for the use of this clause to cover political lobbying campaigns undertaken by the pharmaceutical industry.

Norgine recognised that as part of general good corporate governance, companies had a responsibility to ensure that any such material was factually accurate and not misleading. Norgine had been scrupulous in this regard, and where it was the originator of material on the issue of generic substitution, took care about the content of material it sponsored and its role. The Consensus Document 'Automatic Generic Substitution – Clinical implications for patients', was sponsored by Norgine as clearly declared in that document. All parties involved in that document were told of Norgine's role as sponsor.

Norgine noted the Panel's view as expressed in its ruling that the majority of those reading the letter in The Times would have viewed it differently if they had known that it was indirectly associated with Norgine's opposition to generic substitution and, in a limited way, had been facilitated by a pharmaceutical company with an interest in the views expressed.

Norgine submitted that it could not say whether this was true or not. Norgine expected most people to judge the letter by reference to the force of the points it made. Norgine was not alone in having an interest in the views expressed and, therefore, it was not critical that Norgine's interest in the letter was explained in it. The Government was currently considering the outcome of a formal public consultation on these proposals (provided). Significant opposition to generic substitution had been expressed by groups representing patients, doctors and pharmacists who responded to the consultation (provided).

Norgine did not think that readers would look at the content of the letter any differently had they known about the limited involvement of Norgine. Pharmaceutical companies had a degree of expertise in the arrangements for the supply of medicines, so the arguments made in the letter would be seen as equally valid if readers were informed of company involvement.

Norgine observed that if it were necessary for the letter to refer to the alleged 'sponsorship' by Norgine, the Code would require not just the fact of such 'sponsorship' but also the nature of it to appear. The authors would have a legitimate interest in making sure that readers knew that the views they expressed were honestly held and they had not been coerced by Norgine into writing it or paid for their time in writing it. The statement of sponsorship required where the involvement of Norgine was so limited and tangential would have involved text disproportionate to the main text of the letter itself, and might have meant that The Times would not have printed it, which would have been an unfortunate consequence. This was a clear pointer to the fact that, even if - contrary to Norgine's main point - lobbying on health policy fell within the Code, it would be wholly disproportionate to the aims of Clause 9.10 to require a statement of sponsorship in these circumstances. Furthermore, the letter which appeared in The Times was substantially rewritten from the first draft authored by the PR agency (drafts provided).

Norgine reiterated that this type of activity was outside the scope of the Code. There were numerous precedents where pharmaceutical companies would have been involved to a greater or lesser extent in facilitating this sort of letter in reference to health and medicines policy in general, yet no indication of company involvement was treated as required.

In a situation where a letter in the medical or lay press related to a specific medicine and a pharmaceutical company was involved in providing information, disclosure of the role of an individual company or companies was not usual, despite the fact that this sort of activity would on the arguments made by the Panel in this case be within the scope of the Code.

Clause 23.2

Clause 23.2 contained a general statement that 'When working with patient organisations, companies must ensure that the involvement of the company is made clear and that all of the arrangements comply with the Code'. It then went on to refer to the Code requirements that were engaged. Norgine submitted that it did not create a free standing obligation that was not specified elsewhere in that clause or elsewhere in the Code. In that respect it was unlike the original Clause 20.3, which at the time, was the only provision relating to the interaction between industry and patient organisations such that all obligations were encompassed within Clause 20.3. The only breach of requirements alleged by the Panel was the breach of the sponsorship acknowledgement in Clause 23.8. Therefore, Norgine did not consider that the Panel was correct to treat Norgine as separately in breach of Clause 23.2. Norgine, therefore, addressed the substance of the complaint under Clause 23.8 below and denied any separate breach of Clause 23.2.

Clause 23.8

Norgine submitted that its lobbying activities, and the letter at issue, was outside the scope of the Code. Furthermore, it denied that its limited role in helping the authors of the letter agree the text of it, was 'working with patient organisations' in a way that the provision was intended to cover such that a 'sponsorship' of the decision of the patient association representative to sign the letter needed to be declared.

Norgine was not cavalier about such matters. In relation to the production of the Consensus Document, its view of the scope of the Code did not affect the care it exercised in its interactions on this issue with patient organisations and their representatives. This was made clear in Norgine's response to the Panel, and it affirmed its commitment to this principle.

The declaration of sponsorship in respect of that document stated: 'The document was researched using interviews with healthcare providers, patient associations and published literature, and drafted by a medical writer [identified] funded by Norgine'.

Norgine submitted that in this campaign, its PR agency, acting as its agent and consistent with its own written ethical policies, ensured that Norgine's involvement was transparent and made clear from the very first contact and throughout the process. The agency's relationship with patient organisations was two-fold. Firstly, the agency supplied patient organisations with background information to enable them to assess and respond to the generic substitution proposals and the subsequent DoH public consultation. Secondly, the agency assisted in the process of identifying which individual clinicians and patient organisations shared Norgine's concern about the proposed change in policy in relation to the dispensing of prescribed medicines and would support and put their name to the Consensus Document. A number of such individuals and patient organisations were identified jointly by Norgine and the agency. The agency thereafter contacted these individuals and individuals representing patient organisations by telephone.

Norgine submitted that it was important to note that it was the agency's policy that in any telephone contact made to an individual with respect to such a campaign, it was made clear that the campaign was being conducted on behalf of a sponsor company, which was always specifically named. The information provided by Norgine and/or the agency was not product or medicines related and had been reviewed internally by Norgine to ensure that this was the case. The information related to health policy and the dispensing of prescribed medicines generally, and the patient safety risks associated with the proposed changes.

Norgine submitted that in contrast to the production of the Consensus Document, the letter to The Times was not an initiative of Norgine, but was a personal

initiative of attendees at the meeting sponsored by Norgine. Norgine did not ask that the letter be written nor pay signatories for their time in writing it. The only contribution Norgine made to its production was that a medical writer from the agency, who had taken notes at the meeting, agreed to do a first draft for the relevant individuals to help them move the matter forward. The authors then contributed to and agreed the text of the letter that the lead signatory submitted to The Times on behalf of himself and the other signatories.

Neither Norgine nor the agency sponsored any of the patient organisations or signatories to the letter. No honoraria, payments or benefits in kind were made to the individual signatories of the letter or patient organisations either directly or indirectly. This was a situation in which Norgine and the individual signatories shared a profound, but independent, concern that the proposed changes in the dispensing of prescription medicines posed an unacceptable patient safety risk and that the public should be made aware of this issue and provided relevant information relating thereto.

Norgine submitted that, therefore, in relation to the letter it did not 'work with' the patient association to further its objectives, and there was no sponsorship of the associations or their representatives. The Panel seemed to recognise the probable lack of any material 'working with' patient associations. In its ruling the Panel had stated: 'The Panel queried whether the letter was developed and produced as a result of a formal interaction between Norgine and the patient organisations or a more personal interaction with individuals operating wholly independently from their patient organisation. However, as patient organisations were named and the senior position of each signatory within the organisation given, there was an implication that each organisation formally endorsed the letter. This would certainly be the impression given to readers'.

Norgine submitted that the Panel was correct as to the first element of this analysis, and it respectfully suggested was wrong to treat the fact that certain individuals decided to sign as representatives of their associations rather than in their purely personal capacity, changed the reality and meant Norgine was 'working with' the patient association. Norgine and the PR agency interacted both with individual health professionals and individuals who were associated with patient organisations. It was not possible to interact with an abstract concept like a 'patient organisation'; one had to interact with individual people.

Norgine submitted that it had no way of knowing at the time, nor would it have been proper for it to enquire, about what involvement these individuals had with their patient organisations. That was wholly a matter for these individuals and their organisations. The signatories determined how their affiliation should appear. This was not a matter for Norgine or the agency given that the content of the letter was outside of its control.

Patient organisations no doubt had their own policies about internal interactions in this sort of situation, and Norgine was very unhappy about the clear suggestion in the Panel ruling that individuals representing patient groups might have improperly taken it upon themselves to represent their patient group.

Norgine noted that the Panel had ruled a breach of Clause 23.8 because Norgine's role was not clear. Notwithstanding its previous arguments as to why this letter was outside the scope of the Code; Norgine submitted that its role was not to work with the patient associations in question in the production of the letter or to 'sponsor' it, and as such on both these counts it rejected the ruling of a breach of Clause 23.8.

Clause 9.1

From the points made above, Norgine reiterated its assertion that this activity was outside the scope of the Code, but nevertheless and, without prejudice, it submitted that both Norgine and its agent had consistently maintained the highest standards with respect to this campaign and in particular the circumstances which led up to the letter in question being published in The Times. Norgine's compliance procedures were rigorously applied, and as described above, Norgine ensured that a responsible level of internal review was conducted even in circumstances where such scrutiny was not required. As such Norgine rejected any breach of Clause 9.1.

Moreover, even if the Appeal Board found that the letter was within the scope of the Code, which Norgine firmly believed was not the case for the reasons outlined above, to stretch the normal understanding of the Code to find a breach of Clause 9.1 seemed unfair.

Norgine noted that Clause 9.1 stated that 'High standards must be maintained at all times'. This broad wording was interpreted by the Code through connection to Clause 9.2, which read: 'All material and activities must recognise the special nature of medicines and the professional standing of the audience to which they are directed and must not be likely to cause offence'. In fact the Code provided combined supplementary information to both Clauses 9.1 and 9.2 under the heading 'Suitability and Taste'. The supplementary information to Clauses 9.1 and 9.2 stated that:

'The special nature of medicines and the professional audience to which the material is directed require that the standards set for the **promotion of medicines** are higher than those which might be acceptable for general commodity **advertising.**

It follows therefore that certain types, styles and methods of **promotion,** even where they might be

acceptable for the **promotion** of products other than medicines, are unacceptable' (emphasis added).

Norgine submitted that it appeared from the wording of the supplementary information set out above that Clauses 9.1 and 9.2 applied to the inappropriate promotion of medicines and not to non-promotional activities or materials. Moreover, it also followed from the supplementary information to these two clauses that in principle, the term 'high standards' was interlinked to the concepts of 'good taste' and 'what was likely to cause offence'. The examples given in this supplementary information reinforced this interpretation as they all related to activities that, in the context of the promotion of medicines, would be considered in poor taste and/or could cause offence to the recipients.

Norgine accepted, however, that Clause 9.1 had been applied to non-promotional activities governing statements about specific medicines and that on occasions, this might be reasonable, particularly where company procedures were seen to be so lax that they resulted in obvious breaches of the Code.

However, Norgine submitted that this was not the case in this instance. Norgine had not issued information in poor taste or likely to cause offence. Nor had it issued inconsistent or incomplete information indicative of poorly executed procedures. This letter was agreed not to concern an issue of promotion or even a non-promotional piece about a specific identified medicine. It concerned health policy and it could not be said that the decision of the Panel involved a straightforward application of the sponsorship provisions.

If, contrary to Norgine's primary contention that these activities were outside the Code and the Appeal Board considered the letter in question and Norgine's involvement in it being issued was within the Code, the case raised a discrete issue not clearly addressed in the Code or supplementary information to it. Where the standard was not clearly established in relation to an activity, it was difficult to see how a finding of failure to meet high standards was fair. Clause 9.1 was seemingly intended to address serious breaches, particularly involving the use of promotional pieces in poor taste or likely to cause offence and which, therefore, did not adequately reflect the special responsibility imposed upon pharmaceutical companies when issuing material relating to their products. This was not such a case and a breach of Clause 9.1 was not appropriate.

Summary

Norgine submitted that if the Appeal Board ruled, that the letter to The Times was outside the scope of the Code, then the Panel's rulings could not stand.

Whilst the Panel and the complainant might consider that the public would like to know more about the background to such a letter, the reality was that the Code did not require any further disclosure. Whilst some might like/want to know certain information or find it of interest, that was not the question before the Appeal Board. The question was whether the letter came within the scope of the Code, and the answer, was 'no'. To find otherwise, no matter how seemingly attractive that proposition, would stifle political lobbying activities on issues of general health policy and patient safety.

Moreover, even if the Appeal Board was to find a breach of Clause 9.10, it would be an unacceptable stretch to find a breach of Clause 9.1. Similarly, Norgine contended that there was no separate breach of Clause 23.2 and no breach on the facts of Clause 23.8. Clauses 23.2 and 23.8 did not give rise to independent breaches and a multiplication of complaints arising out of the same alleged breach would be an unacceptable extension.

Finally, Norgine had grave concerns about the ability of the Panel in the first instance, and ABPI members generally, to impartially rule upon alleged breaches of the Code arising out of a letter critical of a policy of which the ABPI was the proponent. This was not an aspect of the Code that reflected laws relating to promotion, but reflected the separate policy of ABPI members. The inherent conflict of interest was manifest and transparent to Norgine, yet the vested interests of the adjudicating bodies was not transparent to the public. The Panel itself, in rendering its decision, should have been transparent to the public, by disclosing the interests of its affiliated members in promulgating the policy of automatic generic substitution, of which the letter was disparaging and which policy, Norgine had vociferously condemned.

COMMENTS FROM THE COMPLAINANT

The complainant stated that the bottom line was that the letter to The Times letter would not have existed were it not for the activities of the PR agency, employed by Norgine, and Norgine's instructions to it. This was not transparent in the letter in The Times, which was misleading. This was not a spontaneous out-pouring of concern.

The complainant had emails showing that the initial contact from at least one signatory was via the agency, and verbal confirmation of this from another. As far as the complainant could see, the agency co-ordinated the signatories. This wasn't clear in the published letter. Had Norgine included a signatory from itself at least it would have been clear that there was pharmaceutical company involvement. Norgine did not and the complainant alleged that this brought the status of pharma into disrepute.

The complainant stated that it was a bit silly to use 'facts' as a synonym for 'information'. The point about 'information' was that it was unverified, and was prone to bias. The letter to the Times was information about prescription medicines – information which was alarmist about generic

prescribing and provided many views on prescribing. Of course it should be covered by the Code.

The complainant submitted that there was no evidence at all that people had or had not felt misled by the omission of a signatory from Norgine. The argument that this inclusion would have meant that The Times would not have printed it proved the point that this was not an 'ethical' letter – ie that being 'truthful' would lead to non publication.

The complainant noted that it seemed that the letter was written by an agency employee after discussions, for the approval of signatories, who were also being sought by the agency in tandem and who had not always been involved in meetings organised by the agency at the start of the campaign. This letter would not have been published without the co-ordination of the agency, and thus Norgine. Journalists (whom the complainant presumed were paid to be present) at meetings with the agency – which was organised to suggest ways forward – opined that a letter be written. The letter was then drafted by an agency employee. Then the agency co-ordinated the letter and the signatories. To suggest that this was not an initiative of Norgine seemed rather baseless.

The complainant explained that she became interested in this letter because it appeared to be spontaneous which the complainant thought was unusual, even strange. That was why she had contacted people to see why they had signed the letter. Initially, the complainant thought that she might have missed something – having been very much 'pro' generics – why were so many people in disagreement with her? It became clear, on asking the people who responded (and not all did, stating in the BMJ rapid responses that the complainant should have made it clear she was a writer – as though an ordinary member of the public should expect less response) that the origin of this letter was part of an orchestrated campaign. Of that, the complainant had no real objections – free speech and liberty – except that of transparency. Had Norgine put its name to the letter, the complainant would have known the reason for it, and would have confined the newspaper to the recycling bin. When the complainant spoke to Norgine and asked why its name had been missed off, the response was that it considered that it might have 'sullied' the message. The irony was deep and unpleasant.

APPEAL BOARD RULING

The Appeal Board noted that it had first to decide whether the letter published in The Times came within the scope of the Code. Clause 1.1 made it clear that the Code applied to the promotion of medicines to health professionals and to appropriate administrative staff. The Code also applied to certain areas that were non-promotional, including the provision of information to the public about prescription only medicines.

The Appeal Board noted that the letter in question referred to prescribed medicines, it focused on differences between branded and generic medicines and what might happen to patients if pharmacists could automatically substitute a generic medicine even if a specific brand had been prescribed. No medicine was mentioned by name or unique identifying feature. The letter referred a number of times to prescribing and although not explicitly solely about prescription only medicines such medicines would be covered by the letter. Thus, the Appeal Board considered that the letter was subject to the Code as it was information about prescription only medicines aimed at the public.

The Appeal Board noted that the letter to The Times, in contrasting branded and generic medicines, clearly referred to medicines and their uses. The letter had been written as a direct result of a campaign orchestrated by Norgine. Norgine had underwritten the costs of the letter being written. The purpose of Clause 9.10 was to require transparency about pharmaceutical company activities so that readers of the material were aware of any such involvement. The letter itself did not refer to Norgine's involvement and no one from Norgine had signed the letter. In the Appeal Board's view those reading the letter in The Times should have been able to do so in the knowledge that a pharmaceutical company with a vested interest had been involved in its creation. Disclosure in this regard would have allowed the reader to form his own fully informed opinion of the views expressed. The Appeal Board considered that by not making its role clear Norgine had failed to comply with Clause 9.10 and it upheld the Panel's ruling of a breach of that clause. The appeal on this point was unsuccessful.

The Appeal Board noted that the campaign in question was initiated and funded by Norgine. The suggestion that a letter be written to The Times, signed by clinicians and patient organisation representatives, had come from a company-organised roundtable meeting of key journalists to gather their views on how awareness of the issues involved could be raised amongst the general public. Potential signatories to the letter were identified by Norgine or its PR agency; some had been previously identified to sign a consensus document whilst others were contacted only to sign the letter. The Appeal Board noted from Norgine's representatives at the appeal that each signatory chose which title to use when signing the letter; some chose to refer to their role in a named patient organisation ie Chair, President, etc. Individuals with no stated involvement with patient organisations had also signed the letter. The Appeal Board considered that as patient organisations were named, and the senior position of each signatory within the organisation given, readers would assume that each organisation formally endorsed the letter. The Appeal Board considered that in any event, by deliberately not providing any indication of its involvement with the production of the letter, Norgine had not made its involvement with the

patient organisations noted in the letter clear to those reading it. The Appeal Board upheld the Panel's ruling of a breach of Clause 23.2. The appeal on this point was unsuccessful.

The Appeal Board considered that Clause 23.8 required wording to accurately reflect the nature of a pharmaceutical company's involvement in the declaration of sponsorship from the outset. Norgine's role in the development and production of the letter was not made clear to readers of The Times. The Appeal Board upheld the Panel's ruling a breach of Clause 23.8. The appeal on this point was unsuccessful.

The Appeal Board noted that the letter was directed at the public and thus it was important that the public were fully informed as to who was behind it; Norgine, by not declaring its involvement in the creation of the letter had therefore failed to maintain high standards and the Appeal Board upheld the Panel's ruling of a breach of Clause 9.1. The appeal on this point was unsuccessful.

Proceedings commenced	**6 April 2010**
Case completed	**13 August 2010**

CASE AUTH/2310/4/10

NOVO NORDISK v LILLY

Promotion of Byetta

Novo Nordisk complained about Lilly's activities associated with the Diabetes UK Annual Professional Conference which took place 3 – 5 March 2010. At issue were presentations given at a Lilly-sponsored symposium held on the eve of the conference which were alleged to have covered, *inter alia*, the unlicensed use of Byetta (exenatide) with insulin and the development of the once-weekly formulation of exenatide. Novo Nordisk also complained about exhibition panels used by Lilly.

The detailed response from Lilly is given below.

Novo Nordisk noted that the first presentation entitled 'The Association of British Clinical Diabetologists (ABCD) Nationwide Exenatide Audit Update', detailed, *inter alia*, results from patients using Byetta in combination with insulin. This was an off-licence use of Byetta which should have been emphasized by the external speaker and made clear on the related slides. The implication that Byetta could be used in combination with insulin was misleading since this was inconsistent with its summary of product characteristics (SPC).

In inter-company dialogue Lilly described its symposium as a non-promotional forum for the legitimate exchange of medical and scientific information. Novo Nordisk submitted that it was difficult to consider a Lilly-sponsored symposium, which almost entirely focused on the company's marketed and future GLP-1 agonist products, as non-promotional. Nevertheless the fact that during the symposium, whether promotional or not, neither the speaker nor the slides presented declared that the use of Byetta in combination with insulin was not licensed, constituted a breach of the Code.

The Panel noted Lilly's submission that its symposium was to facilitate the legitimate exchange of medical and scientific information. 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 the symposium was alleged to have covered, *inter alia*, the unlicensed use of Byetta with insulin and the development of a once-weekly formulation of exenatide. That the meeting would perhaps elicit interest in these two topics might not necessarily be unacceptable if the arrangements for the meeting and its content satisfied the supplementary information to the Code.

The Panel noted that the Lilly symposium had taken place on the eve of the Diabetes UK Annual Professional Conference. The symposium had been part of the official conference programme although Lilly had chosen not to have it advertised in the official conference programme. The arrangements for the symposium were supplied to, and agreed by, the conference organising committee in advance. The official application form for sponsorship, exhibition stands etc referred to evening symposia and listed Tuesday, 2 March (6-11pm) as an option. Potential attendees had been invited and offered return travel for the meeting and overnight accommodation. The timing of the return journey was flexible depending on the number of days the invitee planned to attend the main conference. There was nothing on the invitation which indicated that recipients had already arranged to attend the main conference. The invitation was headed 'Lilly Annual Diabetes Medical Satellite Symposium at the Diabetes UK 2010 Annual Professional Conference'. Lilly acknowledged that, although unlikely, some of the attendees might not have subsequently attended the main conference. Lilly's meeting began at 5.45pm with drinks and canapés. The scientific session started at 6.15pm and ended at 8.15pm with pre-dinner drinks followed by dinner at 8.30pm. The briefing material for those members of the sales force that would attend the main conference stated 'No Sales Force to attend the symposium'. It was not clear whether this meant that the sales force could nonetheless attend the pre-symposium drinks and the dinner afterwards.

The symposium had taken place in the context of a major UK scientific/clinical conference. In that regard the Panel considered that such conferences might be an appropriate setting for the legitimate exchange of medical and scientific information. Nonetheless, the Panel considered that just because a symposium took place in association with a major conference did not automatically mean that it would be regarded as the legitimate exchange of medical and scientific information.

The Panel noted that Lilly's meeting was by invitation only; the attendee list and invitation process was controlled by Lilly. The Panel considered that the overall impression was that Lilly had organised its own stand-alone meeting, albeit on the eve of a national conference. The invitation included prescribing information for Byetta; it thus appeared that Lilly considered the invitation to the symposium to be promotional. The impression given to invitees might be that Lilly considered the symposium to be promotional. The invitation stated that ABCD

would present further analysis of their exenatide audit. The meeting would also discuss the benefits of glucose and weight control with both current and future GLP-1 receptor agonists and new data comparing GLP-1 receptor antagonists DPP-4 inhibitors. The emphasis would be on how this new information might enhance attendees' current and future clinical practice. In the Panel's view it was extremely difficult to argue that the symposium could take the benefit of the supplementary information to the Code if Lilly considered any part of it to be promotional, requiring prescribing information. Context was important. In stating that it could take the benefit of the supplementary information Lilly had not explained how the material satisfied the requirement of being 'during the development of a medicine'. Exenatide had a marketing authorization. The long acting version did not. In the opinion of the Panel disseminating data to prescribers which potentially expanded a licensed product's market share might be different to the legitimate exchange of medical and scientific information during the development of a medicine which implied debate which enhanced the current state of scientific knowledge. The 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 queried whether the invited audience, GPs with an interest in diabetes and diabetes specialist nurses would participate at the requisite level. In the Panel's view, taking all of the circumstances into account, overall the meeting was a promotional meeting for Byetta; on balance it went beyond being the legitimate exchange of medical and scientific information during the development of a medicine.

The Panel noted that the speaker briefing stated that the objective of the presentation was to present the ABCD audit results on exenatide use in the UK and give a fair and balanced interpretation and analysis of the data. Key points to communicate were to clarify and emphasise the Byetta licence and indications for use and to highlight any off-licence use of Byetta. The Panel noted that in a promotional meeting for a medicine there should be no reference to off-licence use of that medicine. The speaker's attention was drawn to the requirements of the Code. Throughout the presentation exenatide was only referred to by its non-proprietary name and no product or company logos were used. Some slides referred to the 'restricted licence for use of exenatide with insulin and glitazones. Also fear of hypoglycaemia in using exenatide with insulin and sulphonylureas'. In the Panel's view this statement did not promote or encourage the use of exenatide with insulin. The Panel noted, however, that some slides at the end of the presentation referred to the use of exenatide plus insulin and detailed some of the clinical results observed. In a statement from the presenter provided by Lilly, it was noted that these were reserve slides with some limited data on the use of exenatide with insulin, they were not used at the meeting but were available on the ABCD password-protected website for viewing by contributors to the audit.

The Panel considered that Novo Nordisk had to establish on the balance of probabilities that the reserve slides had been used and that the slides used were in breach of the Code. Lilly denied that the reserve slides at issue had been used. Overall, the Panel did not consider that the presentation used at the symposium had been misleading about the licensed use of exenatide nor did it promote Byetta for use in combination with insulin. No breaches of the Code were ruled.

The second presentation, entitled 'Comparison of the Incretin-based Therapies; DDP-4 inhibitors and GLP-1 receptor agonists. An update of recent trial data', referred to exenatide long-acting release (LAR) for once weekly dosing. Exenatide once-weekly was not currently licensed. The new drug application was submitted to the FDA in the US in May 2009. In March 2010 an application was submitted to the European Medicines Evaluation Agency (EMEA). A European licence was not expected for another 12-18 months.

Novo Nordisk noted that this presentation did not clarify (either verbally by the external speaker or on the slides) that exenatide LAR did not have a UK marketing authorization. This misled the health professionals about the regulatory status of the compound. Novo Nordisk suspected that the speaker's had been inadequate and as such Lilly was responsible for the pre-licence promotion of exenatide LAR in breach of the Code.

The Panel noted its comments above regarding the arrangements for and nature of the symposium.

The Panel noted that the speaker briefing stated that the objective of the presentation was to give a fair and balanced presentation of data comparing GLP mimetics vs DPP4 class of therapy. Key points to be communicated were the differentiation of the classes; the presentation of data should be consistent with each medicine's SPC. The speaker was asked to highlight data not considered within the licence and to remind the audience of the licence status if discussing exenatide LAR. The Panel noted Lilly's submission that this was done. The speaker's attention was drawn to the requirements of the Code. Throughout the presentation exenatide was only referred to by its non-proprietary name and no product or company logos were used.

The Panel noted that several of the slides detailed information about exenatide once weekly. The presentation included the results of a study whereby exenatide once weekly demonstrated superior glycaemic control and weight reduction compared with sitagliptin or pioglitazone after 26 weeks' treatment (Bergenstal *et al*). The Panel considered that, in the context of a promotional meeting, the presentation promoted exenatide

LAR prior to the grant of its marketing authorization. A breach of the Code was ruled. None of the slides noted that exenatide LAR was not licensed although Lilly submitted that this information was given verbally by the speaker. On balance the Panel considered that the presentation was misleading with regard to the regulatory status of exenatide LAR. A breach of the Code was ruled. These rulings were appealed. The Appeal Board noted that the title of the symposium organised by Lilly was 'The benefits of GLP-1 Receptor Agonists; current and future therapies'. Invitees were told that the emphasis of the discussions throughout the symposium would be on how the information presented might enhance their present and future clinical practice. In that regard the Appeal Board considered that Lilly appeared to expect the information presented to influence, *inter alia*, current prescribing practice. The Appeal Board further considered that, given the inclusion of prescribing information on the invitation, most attendees would accept the invitation on the basis that the symposium was promotional. In that regard, the Appeal Board noted that the sales force brief referred to the meeting as the 'Byetta Symposium 2010'.

The Appeal Board noted that the speaker briefings given to the Chairman and to the speaker only referred in detail to certain clauses of the Code. The speaker was asked to highlight data not considered within licence and to remind the audience of the licence status if discussing exenatide LAR. The Chairman was asked to ensure any pre-licence therapies were highlighted in the presentations. In the Appeal Board's view these instructions were ambiguous particularly given that the requirements of Clause 3 had not been referred to in detail.

The Appeal Board noted that a high percentage of the slides in the presentation at issue referred to unlicensed medicines/indications. Further, three members of the marketing team had attended the symposium as well as the drinks and dinner.

The Appeal Board rejected Lilly's submission that the symposium constituted the legitimate exchange of medical and scientific information during the development of a medicine and could thus take the benefit of the exemption described in the supplementary information to the Code. In the Appeal Board's view, the symposium, as arranged, was promotional and in that regard the presentation in question promoted exenatide LAR prior to the grant of the marketing authorization. The presentation was misleading with regard to the regulatory status of exenatide LAR. The Appeal Board upheld the Panel's rulings of breaches of the Code.

Novo Nordisk stated that the third presentation, entitled 'The benefits of GLP-1 Receptor Agonists: An overview of future therapies and their data', was delivered by a Lilly employee who did not state that exenatide LAR did not have a marketing authorization. Thus the presentation was misleading in breach of the Code including Clause 2. Novo Nordisk drew parallels with Case AUTH/2234/5/09.

The Panel noted its comments above regarding the arrangements for and nature of the symposium.

The Panel noted that the speaker briefing stated that the objective of the presentation was to provide an overview of current and future data showing the development of GLP-1 receptor agonists and to ensure that the audience knew that exenatide once weekly was currently not licensed. Key points to be communicated were a fair and balanced representation of data around the development of the class and to emphasise that Byetta and Victoza were currently the only licensed GLP analogues available. The speaker's attention was drawn to the requirements of certain clauses of the Code. Throughout the presentation exenatide was only referred to by its non-proprietary name and no company or product logos were used. The presentation gave a positive overview of the development of exenatide once weekly; two slides clearly stated that exenatide once weekly was not currently licensed.

The Panel considered that the presentation promoted exenatide once weekly before the relevant marketing authorization had been granted. The inclusion of statements that the product was not currently licensed were irrelevant in that regard. A breach of the Code was ruled. This ruling was appealed. The Panel considered, however, that the presentation had not been misleading with regard to the regulatory status of exenatide once weekly and in that regard ruled no breach of the Code.

The Panel noted its rulings above that exenatide once weekly had been promoted before the grant of the relevant marketing authorization. The Panel considered that high standards had not been maintained and ruled a breach of the Code. This ruling was appealed. The Panel noted from the supplementary information to Clause 2 that promoting a medicine before the grant of a marketing authorization was an activity likely to be in breach of Clause 2. That clause was reserved as a sign of particular censure. The Panel ruled a breach of Clause 2. This ruling was appealed.

The Appeal Board noted its comments above and that, in its view, the meeting as arranged, was promotional.

The Appeal Board noted the details of the speaker briefing as described above and in particular that there was no mention of the requirements of Clause 3 of the Code.

The Appeal Board considered that the presentation promoted exenatide once weekly before the relevant marketing authorization had been granted. The inclusion of statements that the product was not currently licensed was irrelevant in that regard. The Appeal Board upheld the

Panel's ruling of a breach of the Code.

The Appeal Board noted that the symposium included discussions about the future availability of exenatide LAR and mention was made of the unlicensed use of exenatide with insulin. The Appeal Board further noted that the invitation to the symposium stated that the emphasis of the discussions would be on how the data presented might enhance an attendee's current and future clinical practice. The licence application for exenatide LAR was submitted two days after the symposium. The Appeal Board considered that the attendance of three members of the marketing team added to the impression that the meeting was promotional.

Overall, given the arrangements for and the content of the symposium, the Appeal Board considered that high standards had not been maintained. The Appeal Board upheld the Panel's ruling of a breach of the Code.

The Appeal Board noted from the supplementary information to Clause 2 that promoting a medicine before the grant of a marketing authorization was an activity likely to be in breach of Clause 2. That clause was reserved as a sign of particular censure. The Appeal Board noted its comments above and upheld the Panel's ruling of a breach of Clause 2.

Novo Nordisk noted that Lilly's exhibition panels featured two graphs from Klonoff *et al* (2008). The first graph showed the HbA_{1c} improvement from the core phase of three randomized, controlled trials and their 3-year long, uncontrolled, observational extension period. The graph contained a suppressed zero y-axis to exaggerate the 1% HbA_{1c} decrease revealed by the study. Regardless of no comparator on the graph, this was misleading, and did not maintain high standards.

Novo Nordisk noted that shortening the y-axis exaggerated the observed glycaemic improvement. Lilly's view that health professionals would be able to interpret such results suggested that this type of presentation was acceptable in every case when there was no comparator on the graph. This was clearly not so as this presentation did not give a clear, fair, balanced view of the matter. Further, it had not been stated on the exhibition panel that the analysis was post-hoc. This was an important piece of information to interpret the results correctly and its omission was misleading.

Novo Nordisk noted that more importantly Lilly had not stated that this post-hoc analyzed patient subgroup (n=217) represented only 22.5% of the total patient population exposed to exenatide during the core randomized, controlled phases of the study (n=963). Klonoff *et al* reported that the intention to treat (ITT) population that entered the extension phase was 527, but even in this case the reported graphs represented only 41% of the study population. Knowing this piece of information, one could easily conclude that the paper reported the results from the responders and in fact most patients needed to be switched to other therapies due to the inadequate response to exenatide during the study period. Conversely, without knowing this information, one could conclude that the 1% HbA_{1c} improvement could be sustained with exenatide for 3 years in the general type 2 diabetes population. Clearly the missing pieces of information were highly important and the graphs on the exhibition panels (HbA_{1c} improvement and weight change) misled and failed to maintain high standards.

Novo Nordisk alleged that the graphs were a deliberate attempt to mislead the participants at the largest diabetes scientific event of the UK in breach of Clause 2.

The Panel noted that Lilly's exhibition panel included a graph of the 'Change in HbA_{1c} from baseline in 3 year completer population'. The heading to that section of the exhibition panel was 'Choose BYETTA to provide sustained HbA_{1c} improvement over 3 years'. The x axis plotted weeks of treatment and the y axis was labelled HbA_{1c} (%). The y axis was shortened between 0 to 5% and then showed 5 to 9%. The Panel noted Lilly's submission that the y axis represented a physiological range of HbA_{1c}. The results obtained for Byetta showed that from a baseline of 8.2%, HbA_{1c} fell sharply within the first 26 weeks, and that an initial 1% fall was maintained at week 156. A claim to the right of the graph stated 'Almost half (46%) of patients achieved $HbA_{1c} \leq 7\%$. The graph and the claim were derived from Klonoff et al. Only data for Byetta was shown; there was no comparison with any other medicine.

The Panel noted that clinicians would be familiar with the physiological range of HbA_{1c} and that they would treat patients to a target HbA_{1c} of around 7%. It considered that to shorten the y axis between 0 to 5% did not mean that a suppressed zero was used in a misleading way. The decrease in HbA_{1c} was clearly stated and not exaggerated. The Panel did not consider that the graph was misleading or exaggerated as alleged. In that regard the Panel did not consider that high standards had not been maintained. No breaches of the Code were ruled.

The Panel noted that Klonoff *et al* had taken patients from three placebo controlled trials and their open-label extensions and enrolled them into one open-ended, open-label clinical trial. There had been 527 patients in the ITT population from the three studies; only 217 completed 3 years of exenatide therapy ie only 41% of the original patients. The Panel noted the claim that 'Almost half (46%) of patients achieved $HbA_{1c} \leq 7\%$' referred only to the 3 year completers and so in that regard it was 46% of 41% ie approximately 19%. The Panel considered that the claim implied that almost half of all diabetic patients would achieve $HbA_{1c} \leq 7\%$ with exenatide therapy whereas with

the population studied it was only about 19%. Similarly, claims were made regarding the percentage of patients who would lose weight whilst on exenatide therapy. The Panel considered that with regard to the data from Klonoff *et al*, important information had been omitted from the exhibition panel; the material was not sufficiently complete such as to allow clinicians to form their own opinion of the therapeutic value of exenatide. The Panel considered that the exhibition panel was misleading as alleged. High standards had not been maintained. Breaches of the Code were ruled.

The Panel noted its rulings above and considered that the exhibition panel, although misleading, was not such as to bring discredit upon or reduce confidence in the pharmaceutical industry. No breach of Clause 2 was ruled.

Novo Nordisk complained about the promotion of Byetta (exenatide) by Eli Lilly and Company Limited at the Diabetes UK Annual Professional Conference which took place in Liverpool, 3-5 March 2010. Matters had not been resolved through inter-company dialogue.

A Lilly-sponsored symposium – The benefits of GLP-1 [glucagon-like peptide-1] Receptor Antagonists; current and future therapies

Lilly explained that the objective of the symposium was to facilitate the legitimate exchange of medical and scientific information with diabetes specialists. In this regard, the symposium was relevant to the purpose of the Diabetes UK conference. Indeed, the latter was reflected in the wide-ranging content of the symposium which included a balanced and fair discussion of other GLP-1 based therapies including liraglutide, taspoglutide, albiglutide and DPP-4 [dipeptidyl peptidase-4] inhibitors. In line with the objective of exchanging scientific data, the meeting included off-licence data, therefore members of the sales team were excluded, including the national sales manager and the Byetta marketing managers. Only health professionals attending the Diabetes UK conference with a valid scientific interest in understanding the benefits of the GLP-1 based treatments were invited to attend. Invitees were then required to register online for the symposium. There was also an onsite registration facility only for those invited guests who had not registered online prior to the symposium.

Lilly submitted that the symposium was consistent with its own standard operating procedures (SOPs) and Clause 3 of the Code which stated that 'The legitimate exchange of medical and scientific information during the development of a medicine is not prohibited provided that any such information or activity does not constitute promotion which is prohibited under this or any other clause'.

Lilly provided a copy of the brief to its sales force team attending the conference indicating that all potential Byetta once weekly discussions be directed to members of the medical team. Also provided was email correspondence from the brand manager discussing communication to the sales force reiterating the company's approach to pre-licence discussions.

In response to a request for further information Lilly submitted that the symposium was part of the Diabetes UK Annual Professional Conference. Lilly booked an official conference satellite symposium for the evening of 2 March for which it paid a fee to the conference organisers. The arrangements for the symposium were supplied to, and agreed by, the conference organising committee in advance. The symposium was not included in the official conference programme. Lilly decided not to have its symposium listed on the conference programme and website.

Lilly explained that its SOP required that attendees to any of its satellite symposia which involved off-licence information needed to be limited and controlled; therefore Lilly opted not to widely advertise its symposium. This helped restrict attendance to suitably qualified health professionals. It was therefore agreed with the conference organisers that Lilly would invite appropriate health professionals to the symposium. The attendee list and invitation process was controlled by Lilly's medical team. Lilly noted that its general sponsorship of the conference was clearly mentioned in the conference guide.

Lilly explained that health professionals who were expected to attend the conference were invited to arrive earlier to attend the symposium. Given the timing of the symposium, and that delegates were expected to attend the main conference the following morning, it was deemed appropriate to provide overnight accommodation on the night of Tuesday 2 March. Return travel to Liverpool, in conjunction with the overnight stay, was provided to allow delegates to attend the symposium and then the conference. Lilly's invitation did not include conference registration and as such attendance at the conference was outside Lilly's remit. It was therefore possible, but unlikely, that some of those who attended the symposium did not subsequently attend the conference. Lilly submitted that thirty-six attendees were reimbursed for travel costs and twenty-five were provided with overnight accommodation.

Lilly submitted that its symposium was a professional meeting held on the occasion of, and in association with, the Diabetes UK Annual Professional Conference. Only health professionals with a valid scientific interest in understanding the benefits of the GLP-1 based treatments, and who Lilly considered would have attended the conference regardless, were invited. Of the suitably qualified diabetes health professionals (consultant diabetologists, diabetes nurse specialists, specialist registrars in diabetes and GPs with a special interest in diabetes) who were expected to attend the conference, 2,170 were invited to attend the symposium. Invitations were initially sent to 240 health professionals but only a

small number were able to attend and so a second, and then third wave of invitations were sent out to health professionals, who met Lilly's criteria. Seventy-three delegates attended the symposium. An attendee list was provided.

1 Presentation – The Association of British Clinical Diabetologists (ABCD) Nationwide Exenatide Audit Update

COMPLAINT

Novo Nordisk noted that an external health professional presented the latest data from the audit as the first speaker of the symposium. Part of the presentation provided results from patients using Byetta in combination with insulin. This was an off-licence use of Byetta which should have been emphasized by the speaker and made clear on the related slides. Novo Nordisk considered that Lilly was responsible for presenting results in relation to the off-licence use of Byetta, without highlighting this important information appropriately to the audience. The implication that Byetta could be used in combination with insulin was misleading since this was inconsistent with its summary of product characteristics (SPC). Novo Nordisk alleged a breach of Clauses 3.2 and 7.2.

In inter-company dialogue Lilly described its corporate symposium as a non-promotional forum for the legitimate exchange of medical and scientific information. Novo Nordisk submitted that it was difficult to consider a Lilly-sponsored symposium, which almost entirely focused on the company's marketed and future GLP-1 agonist products, as non-promotional. Nevertheless the fact that during the symposium, whether promotional or not, neither the speaker nor the slides presented declared that the use of Byetta in combination with insulin was not licensed, constituted a breach of the Code as alleged above.

Novo Nordisk had asked for a copy of the speaker briefing document and the slides in order to assess the measures Lilly took with regard to the data presented concerning this off-licence use. However Lilly had not provided either document although in inter-company correspondence it consistently referred to them.

Novo Nordisk did not understand Lilly's reference in inter-company dialogue to the liraglutide (Victoza) audit, also conducted by the ABCD. Any audit collected data on real life use of the audited product which might cover off-licence use of the medicine. This was a scientifically valid way to collect post-marketing data on the effectiveness of marketed products. Such activities were encouraged by regulatory authorities. The fact that the nationwide exenatide audit revealed a significant proportion of type 2 diabetics using Byetta in combination with insulin was clinically important. Novo Nordisk acknowledged that physicians needed to receive information about this finding, however it was concerned about using and sharing this information with prescribers at a Lilly-sponsored symposium without sufficiently declaring that Byetta was not indicated in combination with insulin.

RESPONSE

Lilly submitted that the external speaker, a member of the ABCD steering group, presented the results of a nationwide clinical audit on the use of Byetta in clinical practice. The independent audit was designed, undertaken, implemented and published by the ABCD with administrative and IT support funded by Lilly under a partnership agreement.

In anticipation that the audit also investigated the extent to which health professionals used Byetta off-licence with insulin, Lilly's briefing required the speaker to appropriately highlight that such use of Byetta was unlicensed and remind the audience of the precise licensed indication of Byetta. Indeed, the speaker also discussed the place of Byetta in the management of type 2 diabetes with reference to the National Institute for Health and Clinical Excellence (NICE) guidelines which further clarified the licensed indication of Byetta.

Whilst Lilly selected the speaker, other than with respect to the briefing, it did not exert any editorial control or influence over the content of the presentation. As the meeting was non-promotional, it was desirable for Lilly to ensure that the speaker's presentation was, and was seen to be, an independent view and opinion informed by independent research. Lilly noted that the written speaker brief expressly directed the speaker to comply with the Code and present a fair and balanced interpretation and analysis of the audit findings. A copy was provided.

Lilly submitted that it was imperative to highlight that no off-licence use of Byetta in combination with insulin or glitazones was presented by the speaker at this symposium as alleged. Although one of the speaker's slides included the statement '… restricted licence for use of exenatide with insulin and glitazones', in view of the speaker brief given, the speaker kept this slide as a 'backup' and did not present it at the symposium. A statement to confirm this was provided from the speaker.

Lilly denied breaches of Clauses 3.2 and 7.2.

PANEL RULING

The Panel noted Lilly's submission that its annual diabetes medical satellite symposium at the Diabetes UK 2010 annual professional conference was to facilitate the legitimate exchange of medical and scientific information. 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 the symposium was alleged to have covered, *inter alia*, the unlicensed

use of Byetta with insulin and the development of a once-weekly formulation of exenatide. That the meeting would perhaps elicit interest in these two topics might not necessarily be unacceptable if the arrangements for the meeting and its content satisfied the supplementary information to Clause 3.1.

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

The Panel noted that the Lilly symposium had taken place on the eve of the Diabetes UK Annual Professional Conference. The symposium had been part of the official conference programme although Lilly had chosen not to have it advertised in the official conference programme. The arrangements for the symposium were supplied to, and agreed by, the conference organising committee in advance. The official application form for sponsorship, exhibition stands etc referred to evening symposia and listed Tuesday, 2 March (6-11pm) as an option. Potential attendees had been invited and offered return travel to Liverpool for the meeting and accommodation for the night of Tuesday, 2 March. The timing of the return journey was flexible depending on the number of days the invitee planned to attend the main conference. There was nothing on the invitation which indicated that recipients had already arranged to attend the main conference. The invitation was headed 'Lilly Annual Diabetes Medical Satellite Symposium at the Diabetes UK 2010 Annual Professional Conference'. Lilly acknowledged that, although unlikely, some of the attendees might not have subsequently attended the main conference. Lilly's meeting began at 5.45pm with drinks and canapés. The scientific session started at 6.15pm and ended at 8.15pm with pre-dinner drinks followed by dinner at 8.30pm. The briefing material for those members of the sales force that would attend the Diabetes UK conference stated 'No Sales Force to attend the symposium'. It was not clear whether this meant that the sales force could nonetheless attend the pre-symposium drinks and the dinner afterwards.

The Panel noted that the symposium had taken place in the context of a major UK scientific/clinical conference. In that regard the Panel considered that such conferences might be an appropriate setting for the legitimate exchange of medical and scientific information. Nonetheless, the Panel considered that just because a symposium took place in association with a major conference did not automatically mean that it would be regarded as the legitimate exchange of medical and scientific information.

The Panel noted that one of the slides from the presentation on the audit stated that the headlines from the data analysis would be presented at a trilogy of events. These were listed as; DUK [Diabetes UK] satellite symposium 2 March, DUK main meeting 3 March and ABCD Spring meeting 7 May.

The Panel noted that Lilly's meeting was by invitation only; over 2,000 health professionals were invited, seventy-three attended. The attendee list and invitation process was controlled by Lilly. The Panel considered that the overall impression was that Lilly had organised its own stand-alone meeting, albeit on the eve of a national conference. The invitation to the symposium had included prescribing information for Byetta; it thus appeared that Lilly considered the invitation to the symposium to be promotional. The impression given to invitees might be that Lilly considered the symposium to be promotional. The invitation stated that ABCD would present further analysis of their exenatide audit. The meeting would also discuss the benefits of glucose and weight control with both current and future GLP-1 receptor agonists and new data comparing GLP-1 receptor antagonists DPP-4 inhibitors. The emphasis would be on how this new information might enhance attendees' current and future clinical practice. In the Panel's view it was extremely difficult to argue that the symposium could take the benefit of the supplementary information to Clause 3.1 if Lilly considered any part of it to be promotional, requiring prescribing information. Context was important. In stating that it could take the benefit of the supplementary information to Clause 3.1 Lilly had not explained how the material satisfied the requirement of being 'during the development of a medicine'. Exenatide had a marketing authorization. The long acting version did not. In the opinion of the Panel disseminating data to prescribers which potentially expanded a licensed product's market share might be different to the legitimate exchange of medical and scientific information during the development of a medicine which implied debate which enhanced the current state of scientific knowledge. The 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 queried whether the invited audience, GPs with an interest in diabetes and diabetes specialist nurses would participate at the requisite level. The Panel also noted the apparent difficulty of encouraging attendance to the meeting. In the Panel's view, taking all of the circumstances into account, overall the meeting was a promotional meeting for Byetta; on balance it went beyond being the legitimate exchange of medical and scientific information during the development of a medicine.

The Panel noted that the speaker briefing stated that the objective of the presentation was to present the ABCD audit results on exenatide use in the UK and give a fair and balanced interpretation and analysis of the data. Key points to communicate were to clarify and emphasise the Byetta licence and indications for use and to highlight any off-licence use of Byetta. The Panel noted that in a promotional meeting for a medicine there should be no reference to off-licence use of that medicine. The speaker's attention was drawn to the requirements of Clauses 7.2 and 7.4. Throughout the presentation

exenatide was only referred to by its non-proprietary name and no product or company logos were used. Some slides referred to the 'restricted licence for use of exenatide with insulin and glitazones. Also fear of hypoglycaemia in using exenatide with insulin and sulphonylureas'. In the Panel's view this statement did not promote or encourage the use of exenatide with insulin. The Panel noted, however, that some slides at the end of the presentation referred to the use of exenatide plus insulin and detailed some of the clinical results observed. In a statement from the presenter provided by Lilly, it was noted that these were reserve slides with some limited data on the use of exenatide with insulin, they were not used at the meeting but were available on the ABCD password-protected website for viewing by contributors to the audit.

The Panel considered that the parties' accounts differed. The Panel considered that Novo Nordisk had to establish on the balance of probabilities that the reserve slides had been used and that the slides used were in breach of the Code. Lilly denied that the reserve slides at issue had been used. Overall, the Panel did not consider that the presentation used at the symposium had been misleading about the licensed use of exenatide nor did it promote Byetta for use in combination with insulin. No breach of Clauses 3.2 and 7.2 was ruled.

2 Presentation – Comparison of the Incretin-based Therapies; DDP-4 inhibitors and GLP-1 receptor agonists. An update of recent trial data

This presentation referred to exenatide long-acting release (LAR) for once weekly dosing. Lilly explained that exenatide once-weekly was an extended-release medicine for type 2 diabetes designed to deliver continuous therapeutic levels of exenatide in a single weekly dose. Exenatide once-weekly was not currently licensed for use. The new drug application was submitted to the FDA in the US in May 2009 and accepted in July 2009. It was based on data from the DURATION (Diabetes therapy Utilisation: Researching changes in A1C, weight, and other factors Through Intervention with exenatide Once weekly) clinical trial program. In March 2010 a licence application was submitted to the European Medicines Evaluation Agency (EMEA). A European licence was not expected for another 12-18 months.

COMPLAINT

Novo Nordisk noted that this presentation, by another external health professional, detailed results from DURATION-2 without clarifying (either verbally by the speaker or on the slides) that exenatide LAR did not have a UK marketing authorization. This misled the health professionals about the regulatory status of the compound. Although Novo Nordisk had not seen the speaker's brief, despite requesting a copy of it, it seemed that it might have been inadequate and as such Lilly was responsible for the pre-licence promotion of exenatide LAR by the speaker. Novo Nordisk alleged breaches of Clauses 3.1 and 7.2.

Novo Nordisk noted that Lilly had not provided it with copies of the speaker's brief or the slides as requested during inter-company dialogue. It was only these documents which could clarify whether Lilly made appropriate efforts to ensure compliance with the Code in terms of this presentation.

Novo Nordisk stated that it was irrelevant that an external, independent diabetes professor presented the otherwise publically available results to the audience. On a company-sponsored symposium the slides about exenatide LAR should have included a clear statement as to its regulatory status.

Novo Nordisk again noted its concern about Lilly's corporate symposium as a non-promotional, educational event. Novo Nordisk alleged that the detailed discussion about Lilly's future compound constituted pre-licence promotional activity.

RESPONSE

Lilly stated that it provided the speaker, a renowned professor of diabetes, with a written brief to present on the topic of 'Comparison of Incretin-based therapies; DPP-4 inhibitors and GLP-1 receptor agonists. An update of recent trial data'. Given the premise for the Lilly symposium, as discussed above, the inclusion of this presentation was deemed relevant and proportional given that diabetes specialists attending this major specialist/academic meeting would have a legitimate interest in medical and scientific information about products in development including exenatide once-weekly.

Lilly noted that the brief expressly directed the speaker to comply with the Code and present a fair and balanced discussion of the information presented. Indeed, in anticipation that the presentation would discuss, in part, exenatide once-weekly, which was not currently licensed for use, Lilly's briefing required the speaker to appropriately highlight the latter; which was done. A copy of the brief was provided.

Whilst Lilly had selected and briefed the speaker, it had no editorial control or influence over the content of the presentation. Given this meeting was non-promotional it was desirable for Lilly to ensure that the presentation was, and was seen to be, the speaker's own independent view and opinion. Lilly noted that the speaker's presentation included information about the DURATION-2 study which had previously been presented at other conferences of high academic standing such as the American Diabetes Association. Indeed, the results of this particular study were also presented as part of the proceedings of the Diabetes UK conference itself. A copy was provided.

Lilly denied breaches of Clauses 3.1 and 7.2.

PANEL RULING

The Panel noted its comments at point A1 above regarding the arrangements for and nature of the symposium.

The Panel noted that the speaker briefing stated that the objective of the presentation was to give a fair and balanced presentation of data comparing GLP mimetics vs DPP4 class of therapy. Key points to be communicated were the differentiation of the classes; the presentation of data should be consistent with each medicine's SPC. The speaker was asked to highlight data not considered within the licence and to remind the audience of the licence status if discussing exenatide LAR. The Panel noted Lilly's submission that this was done. The speaker's attention was drawn to the requirements of Clauses 7.2 and 7.4. Throughout the presentation exenatide was only referred to by its non-proprietary name and no product or company logos were used.

The Panel noted that several of the slides detailed information about exenatide once weekly. The presentation included the results of a study whereby exenatide once weekly demonstrated superior glycaemic control and weight reduction compared with sitagliptin or pioglitazone after 26 weeks' treatment (Bergenstal *et al*). The Panel considered that, in the context of a promotional meeting, the presentation promoted exenatide LAR prior to the grant of its marketing authorization. A breach of Clause 3.1 was ruled. None of the slides noted that exenatide LAR was not licensed although Lilly submitted that this information was given verbally by the speaker. On balance the Panel considered that the presentation was misleading with regard to the regulatory status of exenatide LAR. A breach of Clause 7.2 was ruled.

APPEAL BY LILLY

Lilly did not believe that the content, context and general arrangements supporting its meeting at the Diabetes UK conference constituted the promotion of Byetta, or the pre-licence promotion of the once-weekly formulation of exenatide such that it could not take the benefit of the supplementary information to Clause 3.1.

Lilly agreed that to determine whether a meeting was promotional or not, the content and context in which it had taken place were important but its intent and purpose should also be considered. The meeting was solely to facilitate the legitimate exchange of medical and scientific information relating to Byetta as well as the once-weekly formulation of exenatide, a new medicine currently in development.

Lilly submitted that as evidenced by the documents previously provided, it had ensured that its medical department owned and controlled the symposium which demonstrated from the outset that the meeting was intended to be non-promotional. The invitation and delegate selection process was carefully controlled by the medical department, the speaker briefings were explicit about the objectives of the meeting and the express requirements of the Code regarding off-licence promotion, the presentations did not use company or product logos and only referred to exenatide by its non-proprietary name. Importantly, sales staff involvement was strictly prohibited. These arrangements clearly demonstrated Lilly's intent to comply with both the letter and spirit of the Code and the non-promotional purpose of the meeting.

Lilly submitted that if it had intended the symposium to be promotional, it would have been controlled by the marketing department and advertised widely; the company would have permitted product branding on the invitations and speaker presentations and allowed the sales force to attend and engage with delegates both at the drinks beforehand and the dinner afterwards.

Lilly submitted that its position that its symposium was non-promotional was supported by the Panel's ruling of no breach of Clauses 3.2 and 7.2 in relation to the alleged promotion of Byetta for use in combination with insulin, outside of its licence at point A1 above. The Panel commented in its ruling that some slides in the presentation 'The Association of British Clinical Diabetologists (ABCD) Nationwide Exenatide Audit Update' referred to the 'restricted licence for use with exenatide with insulins …' but that '[I]n the Panel's view this statement did not promote or encourage the use of …' exenatide outside of its licence. The Panel further commented that '[it] did not consider that [this] presentation … had been misleading about the licensed use of Byetta nor did it promote Byetta for use in combination with insulin'.

Lilly disagreed with the following assertions made by the Panel about the arrangements for and nature of the symposium:

Assertion: Inclusion of Byetta prescribing information on the invitation to the symposium indicated that Lilly considered the invitation to be promotional and created the impression that Lilly considered the meeting to be promotional.

Comment: Lilly noted that the invitation referred to 'The benefits of GLP-1 Receptor Agonists; current and future therapies' and made claims in respect of these. Lilly submitted that Byetta was the first in this class of medicines and data in support of this was to be discussed at the meeting. As such, the Byetta prescribing information was included in the invitation to satisfy Clause 4.1; omission of the prescribing information would have invited a breach of that clause. Lilly therefore disagreed with the Panel's assertion that the inclusion of the Byetta prescribing information indicated that it considered the invitation to be promotional and that, by implication, this might have implied to invitees that Lilly considered the symposium to be promotional.

Notwithstanding the latter, Lilly also referred to established precedents where inclusion of

prescribing information did not automatically render materials promotional; this would be dependent upon their purpose eg invitations to advisory boards. Advisory boards were deemed to be non-promotional by the Code. However, the Code also recognised that prescribing information must form part of the invitation to an advisory board if it mentioned product(s) or a class of medicine to which a product could be easily ascribed and also referred to a claim or indication with respect of these. Similarly the intent and purpose of dissemination of product information to patients via health professionals was also deemed to be non-promotional. In this situation, the dissemination of this data to the health professionals, in the first instance, also necessitated incorporation of the relevant prescribing information. These examples clearly demonstrated that inclusion of prescribing information did not necessarily render a meeting or activity promotional and that the purpose, alongside content and context, was an important consideration.

As stated above, the invitation did not carry the Byetta logo and it only referred to exenatide, its non-proprietary name. If Lilly intended the symposium be to promotional, the invitation would have carried the company and product logos and referred to Byetta, the brand name.

Assertion: The Lilly meeting was deemed to be a standalone symposium because the invitation did not indicate whether recipients had already arranged to attend the main conference and the company's acknowledgement that, although unlikely, some of the symposium attendees might not have subsequently attended the main conference.

Comment: Lilly submitted that its symposium was part of the official conference programme as referred to in the invitation. Whilst the reply to the invitation did not ask recipients to indicate whether they were to attend the main conference, the invitation process clearly anticipated that those who accepted the invitation to the symposium would subsequently attend the main conference. In this regard Lilly noted that of the seventy-three attendees, sixty were officially registered to attend the main conference as evidenced by the pre-published conference delegate list. Of the other thirteen delegates who had not registered to attend the main conference in advance, and whose name would therefore [not] have appeared on the pre-published delegate list, there was a likely possibility that they registered for the conference on the day.

Thus Lilly did not accept that the invitation implied that the company had organised its own standalone symposium, albeit on the eve of a national conference.

Assertion: The Lilly briefing materials which clearly excluded members of the sales force attending the conference from the meeting did not clarify whether this included attendance to the pre-symposium drinks and dinner.

Comment: Lilly submitted that consistent with the purpose of the meeting, all of its representatives attending the conference were specifically excluded from the symposium as well as the pre-symposium drinks and dinner afterwards.

Assertion: Lilly had not explained how the material supporting the discussion of the once-weekly formulation of exenatide could take benefit of the supplementary information to Clause 3.1 particularly in relation to the wording 'during the development of a medicine'.

Comment: The Panel's view was that '… disseminating data to prescribers which potentially expanded a licensed product's market share might be different to the legitimate exchange of medical and scientific information during the development of a medicine …'. Thus the discussion of exenatide, which had a marketing authorization, alongside the once-weekly formulation of exenatide, which did not, entailed promotion of Byetta and, by implication, the once-weekly formulation of exenatide.

Lilly submitted that the Panel ruling implied that the once-weekly formulation of exenatide could not be considered to be a medicine in development and that therefore the discussion of the once-weekly formulation of extenatide was inconsistent with the legitimate exchange of medical and scientific information which was permissible during the development of a medicine when undertaken in the context of a major UK clinical/scientific conference such as the conference in question.

Lilly submitted that the once-weekly formulation of exenatide was currently under development and a European licence had been applied for. The once-weekly formulation of exenatide was a new medicine and was being evaluated as such by the regulatory authorities; it was not a line extension. Therefore, in the context of the conference and the symposium, discussion of data from the ongoing DURATION clinical trial program was legitimate and could not be said to have promoted or expanded the market share of Byetta or the once-weekly formulation of exenatide prior to the grant of its marketing authorization.

Assertion: The invited audience, GPs with a specialist interest in diabetes and diabetes specialist nurses, could not participate in '… debate which enhanced the current state of scientific knowledge' and it was questionable whether they '… would participate at the requisite level'.

Comment: Lilly submitted that the meeting was a closed professional meeting and only those health professionals either known to be attending or expected to attend the conference with a valid scientific interest in gaining an understanding of the benefits of the GLP-1 based treatments were invited. In this regard, the audience appropriately reflected the important role that both primary and secondary care health professionals played in the management of type 2 diabetes. The Panel ruling

asserted that only delegates attending the main conference were likely to participate at the requisite level. This was somewhat inconsistent with the fact that the majority of delegates attending the meeting also attended the main conference. It was therefore reasonable to assume that these particular delegates would have participated at the requisite level required by both meetings.

Lilly submitted that the symposium was to facilitate the legitimate exchange of medical scientific information, and this was evident by the many questions from the audience to the three speakers and meeting chair. This interaction was consistent with the level of debate and discussion expected of such a meeting and which enhanced the scientific knowledge amongst the delegates. Thus the symposium clearly offered the facility for the legitimate exchange of medical and scientific information.

Indeed, if the symposium had been open to all conference delegates, the potentially larger number of attendees might have diluted the focus and substance of the debate and discussion that took place at the meeting. This was clearly not Lilly's intent or the purpose of the symposium.

Assertion: That over 2,000 health professionals were invited and only seventy-three attended implied an apparent difficulty of encouraging attendance to the symposium.

Comment: Lilly reiterated that the invitation process was phased and controlled by the medical department; it was not a single mailing as would have been the case for a promotional symposium. The process allowed the medical department to control the number and specialism of the health professionals invited as well as to carefully monitor the replies and subsequent delegate numbers.

Lilly submitted that a large number of invitations were sent because Lilly needed to ensure that only suitably qualified diabetes health professionals, who expected to attend the conference, were invited. The final number of delegates did not reflect the difficulty of encouraging attendance to the symposium but further demonstrated that the symposium was not intended to be promotional; it was to ensure that the meeting could take the benefit of the supplementary information to Clause 3.1, facilitating debate and the legitimate exchange of medical and scientific information at the requisite level.

With regard to the Panel's rulings, Lilly submitted that the meeting was always intended and set up to be non-promotional and, as such, the legitimate exchange of scientific and medical information, ie the presentation of Bergenstal *et al* was permitted. As Lilly did not agree that the symposium was promotional, it appealed the Panel's ruling that the presentation promoted the once-weekly formulation of exenatide in breach of Clause 3.1.

Lilly submitted that the speaker referred to the regulatory status of the once-weekly formulation of exenatide as expressly required by the speaker briefing. The presentation must be considered as a whole, the speaker's slides as well as what was said, thus Lilly disagreed with the Panel's ruling that, on balance, the presentation was misleading. Lilly maintained that the speaker clearly stated that the once-weekly formulation of extenatide was not licensed.

Lilly also noted that the importance attached by the Panel in its ruling regarding the requirement to include a statement about the regulatory status of the once-weekly formulation of exenatide in the presentation slides themselves appeared to be negated by its ruling of a breach of Clause 3.1 at point A3. In that ruling the Panel stated that 'The inclusion of statements that the product exenatide LAR was not currently licensed were irrelevant …'. This was inconsistent with the Panel's comment at point A2 that 'None of the slides noted that exenatide LAR was not licensed …'. Lilly therefore appealed the Panel's ruling of a breach of Clause 7.2.

COMMENTS FROM NOVO NORDISK

Novo Nordisk had no comments upon Lilly's reasons for appeal.

FURTHER RESPONSE FROM LILLY

During the submission of presentation slides for its appeal Lilly noted that in error, in its response, it had stated that, in line with the objective of exchanging scientific data the meeting included off-licence data, therefore members of the sales team were excluded, including the national sales manager and the Byetta marketing managers. Lilly stated that this clearly suggested that, *inter alia* no exenatide marketing managers were present at the satellite symposium. That was not so: whilst no representative or sales managers were present three members of the marketing department were at the satellite symposium (and the drinks beforehand, as well as the drinks and dinner afterwards). Lilly understood that those concerned took no part in the proceedings and were solely there for the purpose of relationship building.

FURTHER COMMENTS FROM NOVO NORDISK

Novo Nordisk submitted that the presence of the members from the marketing department further confirmed the promotional nature of the symposium. 'Relationship building' by marketeers was a promotional activity based on the ultimate aim of the marketing department to sell the company's products. In addition, Novo Nordisk queried whether they had any responsibility for the management of the sales force. If they had, then effectively a sales function of the business was present at the symposium.

Novo Nordisk submitted that slide 5 of the briefing material about the meeting clearly stated that members of the sales force could not attend the symposium itself. The symposium – according to

the heading of the slide - was defined as the activities between 5.45 – 7.30pm (interestingly the bullet points defined it differently). However the symposium ended with dinner and the document did not cover whether members of the sales force were able to attend this social activity which was clearly an integral part of the event. The wording of this slide suggested that the sales force had the chance to attend the dinner with their customers to build further relationships and potentially to discuss exenatide LAR data. In fact the overview of the week (slide 3) distinguished between the symposium and the dinner which further confirmed that the specific instruction for the sales force to not attend the symposium strictly related to the symposium itself and they were allowed to meet the customers during dinner.

Novo Nordisk further submitted that the internal document did not specify the involvement of the marketing department in the social activity parts of the symposium.

Novo Nordisk submitted that according to the activity briefing document the purpose of the meeting was 'To discuss the benefits of current/future GLP-1 receptor agonists together with the audit data & GLP-1R agonists v DPPIV's with an audience of experts'. That the meeting consisted not only of the symposium but the pre-symposium drinks and moreover the pre-dinner drinks and the dinner itself, suggested that Lilly aimed to specifically discuss exenatide LAR during the social part of the event. On the basis of the evidence provided by Lilly, it was impossible to exclude the presence of members of the sales force and marketing department during the dinner which raised further serious concerns as to whether the company actually organised the event in a non-promotional manner.

Novo Nordisk noted that with regards to the briefing document given to the chairman of the symposium, Lilly emphasised Clauses 7.2 and 7.4 as the relevant clauses of the Code but failed to highlight the importance of Clause 3.1 (from an exenatide LAR perspective) and Clause 3.2 (from the perspective of the combination of exenatide and insulin).

On the basis of the above, Novo Nordisk submitted that the new evidence produced by Lilly further confirmed that the symposium was promotional.

APPEAL BOARD RULING

The Appeal Board noted that the title of the symposium organised by Lilly was 'The benefits of GLP-1 Receptor Agonists; current and future therapies'. Invitees were told that the emphasis of the discussions throughout the symposium would be on how the information presented might enhance their present and future clinical practice. In that regard the Appeal Board considered that Lilly appeared to expect the information presented to influence, *inter alia*, current prescribing practice. The Appeal Board further considered that, given the inclusion of prescribing information on the invitation, most attendees would accept the invitation on the basis that the symposium was promotional. In that regard, the Appeal Board noted that the sales force brief referred to the meeting as the 'Byetta Symposium 2010'.

The Appeal Board noted that the speaker briefings given to the Chairman and to the speaker only referred in detail to Clauses 7.2 and 7.4. The speaker was asked to highlight data not considered within licence and to remind the audience of the licence status if discussing exenatide LAR. The Chairman was asked to ensure any pre-licence therapies were highlighted in the presentations. In the Appeal Board's view these instructions were ambiguous particularly given that the requirements of Clause 3 had not been referred to in detail.

The Appeal Board noted that a high percentage of the slides in the presentation at issue referred to unlicensed medicines/indications. Further, three members of the marketing team had attended the symposium as well as the pre-symposium drinks and the post-symposium dinner.

The Appeal Board rejected Lilly's submission that the symposium constituted the legitimate exchange of medical and scientific information during the development of a medicine and could thus take the benefit of the exemption described in the supplementary information to Clause 3. In the Appeal Board's view, the symposium, as arranged, was promotional and in that regard the presentation in question promoted exenatide LAR prior to the grant of the marketing authorization. The presentation was misleading with regard to the regulatory status of exenatide LAR. The Appeal Board upheld the Panel's rulings of breaches of Clauses 3.1 and 7.2 of the Code. The appeal on this point was thus unsuccessful.

3 Presentation – The benefits of GLP-1 Receptor Agonists: An overview of future therapies and their data

COMPLAINT

Novo Nordisk noted that in this session a Lilly employee detailed the results from DURATION-1 without stating that exenatide LAR did not have a marketing authorization. Thus the presentation was misleading, in breach of Clauses 3.1 and 7.2.

In inter-company dialogue Lilly claimed that appropriate briefing was provided to the speaker to comply with the Code, however Lilly had not sent the briefing material or the slides to Novo Nordisk to substantiate its claims.

Novo Nordisk referred to Case AUTH/2234/5/09 in which Lilly had complained about Novo Nordisk's promotion of liraglutide. As issue in that case had been a symposium, organised by Novo Nordisk at the University of Nottingham, to cover clinically relevant topics for a diabetes specialist nurse

audience. A topic of the agenda was covered by a world-wide known scientific expert on GLP-1, a Novo Nordisk employee who presented data on liraglutide in March 2009 before liraglutide was granted its marketing authorization by the EMEA. Lilly alleged that the presentation promoted the product, and misleadingly implied that liraglutide was a licensed and relevant treatment option for the management of diabetes. The Panel considered the meeting was promotional because it was sponsored by Novo Nordisk and as a result ruled to be in breach of Clauses 2, 3.1, 7.2 and 7.3.

Novo Nordisk considered that Lilly's presentation now at issue, by a Lilly employee who did not clarify the licence status of exenatide LAR should be judged similarly as Case AUTH/2234/5/09 and as such Novo Nordisk alleged a breach of Clauses 9.1 and 2.

Novo Nordisk noted that in inter-company dialogue it gave Lilly the opportunity to address the above mentioned matters and requested copies of the three presentations and the related speaker briefings. Although Lilly referred to the requested materials in its response it did not provide the documents to Novo Nordisk. This blatant lack of response to a clear request in inter-company dialogue was very concerning, and suggested that Lilly deliberately withheld information from Novo Nordisk.

RESPONSE

Lilly explained that its US employee, an eminent diabetologist and expert in GLP-1 based therapies, was provided with a written speaker brief by Lilly in the UK to present on the topic of 'The benefits of GLP-1 Receptor Agonists: An overview of future therapies and their data'. As per Lilly policy the speaker was aware of the requirements of the Code and that the presentation should be accurate and objective, consistent with SPC (where applicable), balanced and capable of substantiation. Indeed, the speaker brief also clearly addressed this requirement. In anticipation that the presentation would discuss, in part, exenatide once-weekly, which was not currently licensed, Lilly's briefing required the speaker to appropriately highlight the latter; which was done. Indeed, contrary to Novo Nordisk's allegation, the presentation included statements to clarify this; initially at the onset of the exenatide once weekly data presentation (slide entitled Development of Exenatide Once Weekly, bullet point 2) and also in the final summary slide of the whole presentation (entitled Conclusions, bullet point 4). Lilly therefore refuted the allegation that this presentation was in breach of Clauses 3.1 and 7.2.

Lilly noted that the speaker's presentation was based on information from the DURATION-1 study that had been previously published in a peer reviewed publication (Drucker *et al* 2008). Lilly provided a copy of the presentation and of the speaker's brief.

Lilly denied a breach of Clauses 9.1 and 2.

PANEL RULING

The Panel noted its comments at point A1 above regarding the arrangements for and nature of the symposium.

The Panel noted that the speaker briefing stated that the objective of the presentation was to provide an overview of current and future data showing the development of GLP-1 receptor agonists and to ensure that the audience was aware that exenatide once weekly was currently not licensed. Key points to be communicated were a fair and balanced representation of data around the development of the class and to emphasise that Byetta and Victoza were currently the only licensed GLP analogues available. The speaker's attention was drawn to the requirements of Clauses 7.2 and 7.4. Throughout the presentation exenatide was only referred to by its non-proprietary name and no company or product logos were used. The presentation gave a positive overview of the development of exenatide once weekly and the clinical results observed; two slides clearly stated that exenatide once weekly was not currently licensed.

The Panel considered that the presentation promoted exenatide once weekly before the relevant marketing authorization had been granted. The inclusion of statements that the product was not currently licensed were irrelevant in that regard. A breach of Clause 3.1 was ruled. The Panel considered, however, that the presentation had not been misleading with regard to the regulatory status of exenatide once weekly and in that regard the Panel ruled no breach of Clause 7.2.

The Panel noted its rulings above, and at point A2, that exenatide once weekly had been promoted before the grant of the relevant marketing authorization. The Panel considered that high standards had not been maintained and ruled a breach of Clause 9.1. The Panel noted from the supplementary information to Clause 2 that promoting a medicine before the grant of a marketing authorization was an activity likely to be in breach of Clause 2. That clause was reserved as a sign of particular censure. The Panel ruled a breach of Clause 2.

APPEAL BY LILLY

Lilly repeated its general comments in its appeal at point A2 above about the arrangements for and nature of the symposium.

Lilly noted that the Panel had ruled a breach of Clause 3.1 in that the presentation at issue promoted the once-weekly formulation of exenatide before the relevant marketing authorization had been granted. The Panel acknowledged in its ruling that the presentation contained two slides which clearly stated that the once-weekly formulation of exenatide was not currently licensed.

Further, Lilly submitted that in the context of a non-promotional meeting, the presentation of an

overview of the development of the once-weekly formulation of exenatide, a new medicine, and the clinical results observed during its development amounted to the legitimate exchange of scientific and medical information such that it could take the benefit of the supplementary information to Clause 3.1 of the Code. For these reasons, Lilly appealed the Panel's ruling of a breach of Clause 3.1.

Lilly noted that the Panel ruled that high standards had not been maintained in that the once-weekly formulation of exenatide had been promoted before the grant of the relevant marketing authorization in breach of Clause 9.1 and that this also amounted to a breach of Clause 2.

For all the reasons set out above, Lilly disagreed with the Panel's assessment that the meeting was promotional and that, as a result, the content of the two presentations referred to in the Panel's ruling above amounted to the pre-licence promotion of the once-weekly formulation of exenatide.

Lilly submitted that at all times the intent and the purpose of the symposium was not to circumvent the requirements of the Code, including Clause 3; organised by its medical department, it was a genuine and serious attempt to engage health professionals in the legitimate exchange of medical and scientific information of value thereby further enhancing their knowledge and understanding of the management of type 2 diabetes. Lilly therefore appealed the Panel's rulings of breaches of Clauses 2 and 9.1.

COMMENTS FROM NOVO NORDISK

Novo Nordisk had no comments upon Lilly's reasons for appeal.

APPEAL BOARD RULING

The Appeal Board noted its comments at point A2 and that, in its view, the meeting as arranged, was promotional.

The Appeal Board noted that the speaker briefing stated that the objective of the presentation was to provide an overview of current and future data showing the development of GLP-1 receptor agonists and to ensure that the audience was aware that exenatide once weekly was currently not licensed. Key points to be communicated were a fair and balanced representation of data around the development of the class and to emphasise that Byetta and Victoza were currently the only licensed GLP analogues available. The speaker's attention was drawn to the requirements of Clauses 7.2 and 7.4 but again, as in point A2 above, there was no mention of the requirements of Clause 3. The presentation gave a positive overview of the development of exenatide once weekly and the clinical results observed; two slides clearly stated that exenatide once weekly was not currently licensed.

The Appeal Board considered that the presentation promoted exenatide once weekly before the relevant marketing authorization had been granted. The inclusion of statements that the product was not currently licensed was irrelevant in that regard. The Appeal Board upheld the Panel's ruling of a breach of Clause 3.1. The appeal on this point was unsuccessful.

The Appeal Board noted that the symposium included discussions about the future availability of exenatide LAR and mention was made of the unlicensed use of exenatide with insulin. The Appeal Board further noted that the invitation to the symposium stated that the emphasis of the discussions would be on how the data presented might enhance an attendee's current and future clinical practice. The Appeal Board noted that the licence application for exenatide LAR was submitted two days after the symposium. The Appeal Board considered that the attendance of three members of the marketing team added to the impression that the meeting was promotional.

Overall, given the arrangements for and the content of the symposium, the Appeal Board considered that high standards had not been maintained. The Appeal Board upheld the Panel's ruling of a breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board noted from the supplementary information to Clause 2 that promoting a medicine before the grant of a marketing authorization was an activity likely to be in breach of Clause 2. That clause was reserved as a sign of particular censure. The Appeal Board noted its comments above and upheld the Panel's ruling of a breach of Clause 2. The appeal on this point was unsuccessful.

B Exhibition panels

COMPLAINT

Novo Nordisk noted that Lilly's exhibition panels featured two graphs from Klonoff *et al* (2008). The first graph showed the HbA_{1c} improvement from the core phase of three randomized, controlled trials and their 3-year long, uncontrolled, observational extension period. The graph contained a suppressed zero y-axis to exaggerate the 1% HbA_{1c} decrease revealed by the study. Regardless of no comparator on the graph, this was misleading, and did not maintain high standards in breach of Clauses 7.2, 7.8 and 9.1.

In inter-company dialogue, Lilly claimed it was acceptable to use a suppressed zero on the graph since the data were not comparative and health professionals could interpret the 1% HbA_{1c} reduction from clinical perspective. Novo Nordisk disagreed and noted that shortening the y-axis gave a misleading impression and exaggerated the observed glycaemic improvement. The argument that health professionals would be able to interpret such results despite the use of a suppressed zero suggested that this type of presentation was acceptable in every case when there was no comparator on the graph. This was clearly not the

case since this presentation did not give a clear, fair, balanced view of the matter.

Furthermore the lack of detailed information about the study setting was also misleading. In the paper it was clearly emphasized that the analysis was post-hoc which was an important piece of information to interpret the results correctly. This was missing from the exhibition panel.

Novo Nordisk noted that more importantly Lilly had not stated that this post-hoc analyzed patient subgroup (n=217) represented only 22.5% of the total patient population exposed to exenatide during the core randomized, controlled phases of the study (n=963). Klonoff *et al* reported that the intention to treat (ITT) population that entered the extension phase was 527, but even in this case the reported graphs represented only 41% of the study population. Knowing this piece of information, one could easily conclude that the paper reported the results from the responders and in fact most patients needed to be switched to other therapies due to the inadequate response to exenatide during the study period. Conversely, without knowing this information, one could conclude that the 1% HbA_{1c} improvement could be sustained with exenatide for 3 years in the general type 2 diabetes population. Clearly the missing pieces of information were highly important and the graphs on the exhibition panels (HbA_{1c} improvement and weight change) misled and failed to maintain high standards, in breach of Clauses 7.2 and 9.1.

Novo Nordisk considered that the layout of the graphs represented a deliberate attempt to mislead the participants at the largest diabetes scientific event of the UK therefore constituted a breach of Clause 2.

RESPONSE

Lilly stated that the exhibition panel at issue was associated with the Lilly diabetes promotional stand at the Diabetes UK conference. The aspects of the panel which concerned Novo Nordisk referred to and were substantiated by Klonoff *et al*. Klonoff *et al* evaluated the effects of at least 3 years' exenatide therapy on glycaemic control, body weight, cardiometabolic markers and safety. Patients from the three initial 30-week, placebo-controlled studies and their open-label extensions were enrolled into one open-label clinical trial. Patients were randomised to twice daily placebo, 5mcg exenatide, or 10mcg exenatide for 30 weeks, followed by 5mcg exenatide twice daily for 4 weeks, then 10mcg exenatide twice daily for at least 3 years of exenatide exposure. Patients continued metformin and/or sulphonylureas.

The inclusion criteria for the three 30-week, placebo-controlled trials were that patients were between 19 and 70 years of age with type 2 diabetes, treated for at least 3 months prior to screening with at least 1500mg/day metformin, or at least the maximally-effective dose of a sulphonylurea, or a combination of metformin and sulphonylurea. Additional inclusion criteria were an $A_{1c} \leq 11.0\%$ and body mass index of 22-45kg/m. To enrol in the open-label, uncontrolled extensions of the 30-week studies, patients were required to complete the antecedent 30-week placebo controlled trial. Patients completing the extension studies were invited to enrol into the single open-ended, open-label trial analysed in this paper. All patients in this report had been treated with exenatide for at least 3 years, irrespective of their treatment group in the 30-week, placebo-controlled trials.

The 3-year and 3.5-year completer cohorts were defined as all patients who had the opportunity to achieve 3 years or 3.5 years of exenatide exposure, respectively, regardless of their treatment arm in the 30-week placebo-controlled trails. Patient disposition from the beginning of the open-ended, open-label extension trial was as follows: 3-year eligible ITT population (n=527), 3-year completers (n=217) and withdrew (n=310).

Lilly rejected the allegation regarding the suppressed zero on the y-axis of the graph on the basis that the actual published graph also did not employ a zero value for the percentage of HbA_{1c} on the ordinate axis; this axis was labelled as starting from an HbA_{1c} of 4%. The chart shown on the exhibition panel was marked as being 'Adapted from Klonoff DC *et al*' and as such did not include the starting value for HbA_{1c} of 4%. At no stage had Lilly claimed it was acceptable to use a suppressed zero on the graph as alleged by Novo Nordisk.

Notwithstanding the latter, the data represented were not comparative and as such Lilly was confident that diabetologists attending the conference were not misled and would have been able to surmise both the numerical and clinical implication and relevance of a 1% reduction of HbA_{1c} depicted on the exhibition panel irrespective of the labelling on the ordinate axis. To add to this clarity, a blue box highlighting the 1% HbA_{1c} drop was clearly depicted within the graph on the aforementioned panel. Furthermore, the ordinate axis represented a physiological range of HbA_{1c} and as such diabetologists would not be misled if a data point with respect to an HbA_{1c} of 0% was not shown. Indeed, the critical aspect of this chart was the abscissa which depicted the duration over which the reported reduction in HbA_{1c} occurred.

With regard to not stating that the analysis presented was post-hoc, Lilly noted that whilst specific post-hoc analyses were performed at weeks 156 and 182 for the within-group comparisons at endpoint, with sub-analyses by weight change quartiles at weeks 156 and 182, the exhibition panel at issue referred only to results in relation to a priori analyses investigating changes from baseline in HbA_{1c} and body weight in the 3-year completer population and not with reference to the post-hoc analyses involving within-group comparisons at endpoint.

Lilly noted that Novo Nordisk asserted that the non-completer population discussed in this study were

non-responders or patients who had an inadequate response to exenatide therapy and consequently had to be switched to other medicine. This was not so; whilst 310 patients withdrew (ITT vs completers), this was for a variety of reasons and only 18 patients (3%) withdrew due to loss of glucose control whilst on exenatide.

The exhibition panel contained graphs which were clearly titled as 'completer population' to aid clarity. The exhibition panel provided the relevant information pertaining to the 3-year completer population (ie n=217, baseline mean HbA_{1c}: 8.2±0.1%, week 156: -1% (95% CI; -1.1 to -0.8%) and p<0.0001) and these were labelled as being parameters specific only to this particular population. The exhibition panel did not extrapolate the applicability of the results depicted to type 2 diabetic patients in general. Notwithstanding the latter, Lilly noted that the demographics, baseline metabolic parameters reported were typical of type 2 diabetics and not outliers as asserted by Novo Nordisk. This was also evidenced by the authors who in the conclusion stated, without qualification, that '… exenatide represents an option for adjunctive therapy for patients with type 2 diabetes not achieving adequate glycaemic control'.

On all counts, Lilly denied that the exhibition panel was in breach of Clauses 2, 7.2, 7.8 and 9.1. The company also refuted the allegations that the layout of the graph represented a deliberate attempt to mislead health professional and constituted a breach of Clause 2.

In conclusion, Lilly was cognisant of its responsibilities with respect to the Code and had ensured that all aspects of its attendance at the Diabetes UK conference were consistent with this (including, without limitation, Clauses 2, 3.1, 7.2, 7.8 and 9.1) and of the highest standard and quality.

PANEL RULING

The Panel noted that Lilly's exhibition panel included a graph of the 'Change in HbA_{1c} from baseline in 3 year completer population'. The heading to that section of the exhibition panel was 'Choose BYETTA to provide sustained HbA_{1c} improvement over 3 years'. The x axis plotted weeks of treatment and the y axis was labelled HbA_{1c} (%). The y axis was shortened between 0 to 5% and then showed 5 to 9%. The Panel noted Lilly's submission that the y axis represented a physiological range of HbA_{1c}. The results obtained for Byetta showed that from a baseline of 8.2%, HbA_{1c} fell sharply within the first 26 weeks, and that an initial 1% fall was maintained at week 156. A claim to the right of the graph stated 'Almost half (46%) of patients achieved $HbA_{1c} \leq 7\%$. The graph and the claim were derived from Klonoff *et al*. Only data for Byetta was shown; there was no comparison with any other medicine.

The Panel noted that clinicians would be familiar with the physiological range of HbA_{1c} and that they would treat patients to a target HbA_{1c} of around 7%. It considered that to shorten the y axis between 0 to 5% did not mean that a suppressed zero was used in a misleading way. The decrease in HbA_{1c} was clearly stated and not exaggerated. The Panel did not consider that the graph was misleading or exaggerated as alleged. No breach of Clauses 7.2 and 7.8 was ruled. In that regard the Panel did not consider that high standards had not been maintained. No breach of Clause 9.1 was ruled.

The Panel noted that Klonoff *et al* had taken patients from three placebo controlled trials and their open-label extensions and enrolled them into one open-ended, open-label clinical trial. There had been 527 patients in the ITT population from the three studies; only 217 completed 3 years of exenatide therapy ie only 41% of the original patients. The Panel noted the claim that 'Almost half (46%) of patients achieved $HbA_{1c} \leq 7\%$' referred only to the 3 year completers and so in that regard it was 46% of 41% ie approximately 19%. The Panel considered that the claim implied that almost half of all diabetic patients would achieve $HbA_{1c} \leq 7\%$ with exenatide therapy whereas with the population studied it was only about 19%. Similarly, claims were made regarding the percentage of patients who would lose weight whilst on exenatide therapy. The Panel considered that with regard to the data from Klonoff *et al*, important information had been omitted from the exhibition panel; the material was not sufficiently complete such as to allow clinicians to form their own opinion of the therapeutic value of exenatide. The Panel considered that the exhibition panel was misleading as alleged and ruled a breach of Clause 7.2. High standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel noted its rulings above and considered that the exhibition panel, although misleading, was not such as to bring discredit upon or reduce confidence in the pharmaceutical industry. A ruling of a breach of Clause 2 was a sign of particular censure and reserved for such. No breach of Clause 2 was ruled.

Complaint received **7 April 2010**

Case completed **2 November 2010**

CASE AUTH/2312/4/10

ALLERGAN v PFIZER

Promotion of Xalatan

Allergan complained about the promotion of Xalatan (latanoprost) and Xalacom (latanoprost plus timolol) by Pfizer. The items at issue were a POAG (primary open angle glaucoma) Budget Impact Model for Xalatan and Xalacom and a journal advertisement, 'Is your prescribing optimised?'. Allergan supplied Lumigan (bimatoprost) and Ganfort (bimatoprost plus timolol).

Allergan stated that Pfizer's long-standing campaign centred around the loss of patent in July 2011 on Xalatan and Xalacom. The campaign encouraged prescribing of Xalatan or Xalacom now in preference to other medicines, in order to realise future cost savings when they came off patent. Price predictions had been made for the corresponding generic medicines and those of competitors including Lumigan and Ganfort. Annual treatment costs had been calculated based on these projected estimates, which had then been used to arrive at comparative cost-saving claims quoted over a period of up to five years.

Although NHS budget holders would be interested in discussing areas for potential reduction in medicine expenditure it was impossible for Pfizer to accurately forecast generic medicine prices and it certainly could not predict the future pricing behaviour of its competitors. Allergan failed to see how a campaign based on pure speculation could be acceptable. Any cost saving claims so formulated were highly likely to be inaccurate. When extrapolated over a long time period, they became increasingly unsupportable and misleading whilst artificially inflating the potential savings.

Allergan did not consider the statements at the beginning of the model to acknowledge the inability to accurately predict future prices of medicines and to put the responsibility on the customer for any data entered, did not make the principle of the model acceptable.

Allergan also had major concerns about the following statement (or similar) which had featured prominently on all campaign materials, including the budget impact model and advertisement at issue:

> **'The current assumption is that Xalatan and Xalacom will come off patent in the UK in July 2011. However, a paediatric development programme is ongoing in Europe which, if all the requirements of the EU Paediatric Medicines Regulation are met, may result in an extension of 6 months.'**

Allergan believed this statement was teaser advertising and promotion of a medicine outside the terms of its marketing authorization.

The detailed response from Pfizer is given below.

The Panel noted that the advertisement at issue was headed 'Is your prescribing optimised?' below which it stated 'Xalatan and Xalacom will be the first prostaglandins to come off patent'. Readers were told that initiating patients on Xalatan or Xalacom now meant that they had the prospect of realising significant long-term savings when generic versions became available without having to interrupt patient treatment. Readers were invited to find out more. Xalacom and Xalatan were currently more expensive than some of the competitor products and thus initiating patients now on Pfizer's products might mean more expensive treatment costs until July 2011 or January 2012 whenever the products came off patent. It was of course likely that savings would be made once generic versions were available. A footnote explained that the current assumption was that Xalatan and Xalacom would come of patent in July 2011. However, a paediatric development programme was ongoing in Europe, which, if all the requirements of the EU Paediatric Medicines Regulations were met, might result in an extension of 6 months. The Panel thus noted that Xalatan and Xalacom might not come off patent until January 2012 ie almost two years after the advertisement was prepared. In that regard the Panel questioned the use of the claim 'Significant savings are in sight'.

The Panel noted that both the advertisement and the budget impact model which clearly promoted Xalatan and Xalacom, referred to the paediatric development programme. The Xalatan summary of product characteristics (SPC), however, stated that safety and effectiveness in children had not been established. Xalatan was therefore not recommended for use in children. The Panel considered that it was important to give an idea of time scale regarding when the products would come off patent however there was no need to explain the reason why. The Panel considered that the advertisement and the budget impact model insomuch as they also referred to the ongoing paediatric development programme, were inconsistent with the particulars listed in the Xalatan and Xalacom SPCs. A breach of the Code was ruled. The Panel further considered that such promotion of a medicine meant that high standards had not been maintained. A further breach of the Code was ruled.

The Panel did not consider that the statement regarding the paediatric development programme

constituted 'teaser' advertising which was material issued to elicit interest in something which would follow at a later date without providing any information about it. Information about Xalatan and Xalacom had been provided. No breach was ruled in this regard.

The Panel noted that the five year budget impact model compared the acquisition costs of Xalatan and Xalacom with that of its competitors and explored possible five-year cost savings that might be achieved when Xalatan and Xalacom came off patent. The users of the model were informed that: 'The predicted dates for loss of exclusivity (LOE) for [the products featured] are estimates based on current understanding. Please be aware that it is not possible to accurately predict the price of Xalatan, Xalacom, Lumigan, Travatan, Saflutan, Duo Trav and Ganfort post-LOE. The predicted prices will be estimates based on your current understanding, therefore all post LOE prices used in the model are assumptions as selected by you. All analyses within the model that incorporate LOE are therefore also assumptions and may not provide an accurate reflection of the value of Xalatan and Xalacom in the future'.

The Panel noted that by their nature, financial models could only give estimates and that the audience would understand such constraints. The question was whether such estimates were reasonable. The Panel considered that while it might be acceptable for a company to present short-term budget models about its own medicines, over which it could be assumed to have reasonable control, to present a long-term model which generated comparative claims vs competitor products introduced many uncertainties. The model at issue covered five years; the date of the loss of patent for Xalatan and Xalacom was dependent upon the outcome of an ongoing paediatric development programme. The model could be modified to take account that Travatan was expected to come off patent within five years; the prices of generic versions of Xalatan and Xalacom were decided upon by the health professional. Pfizer could not accurately predict competitors' pricing strategies as the dynamics of the market changed. Nor could Pfizer accurately predict government strategy as noted in the model itself, 'Product prices are correct based on the current situation. However prices are subject to change and may go up or down as a result of UK PPRS requirements'. The fact that in the short-term, depending on the date of loss of exclusivity, it would be more expensive to initiate patients on Xalacom and Xalatan than some of the competitors had not been made clear.

Overall, the Panel considered that the budget impact model was based on too many assumptions and uncertainties such that the comparative data generated was too speculative and in that regard it was misleading. The Panel ruled breaches of the Code. The Panel considered that its comments about the budget impact model were relevant in relation to the cost savings claims such as 'significant saving are in sight' in the advertisement and similarly ruled breaches of the Code.

Allergan Ltd complained about the promotion of Xalatan (latanoprost) and Xalacom (latanoprost plus timolol) by Pfizer Limited. The items at issue were a POAG (primary open angle glaucoma) Budget Impact Model for Xalatan and Xalacom and an advertisement in Prescriber, 19 March, 'Is your prescribing optimised?'. Inter-company dialogue had failed to resolve the issues. Allergan supplied Lumigan (bimatoprost) and Ganfort (bimatoprost plus timolol).

COMPLAINT

Allergan stated that Pfizer had run a long-standing campaign centred around the loss of patent in July 2011 of its two major medicines for the treatment of glaucoma, Xalatan and Xalacom. The campaign encouraged health professionals to prescribe Xalatan or Xalacom now in preference to other medicines, in order to realise future cost savings when they came off patent. Price predictions had been made for the corresponding generic medicines and those of competitors including Lumigan and Ganfort. Annual treatment costs had been calculated based on these projected estimates, which had then been used to arrive at comparative cost-saving claims quoted over a period of up to five years.

Allergan acknowledged that NHS budget holders would be interested in discussing areas for potential reduction in medicine expenditure. However Allergan considered that Pfizer's materials used to instigate these discussions did not comply with the Code. It was impossible for Pfizer to accurately forecast generic medicine prices and it certainly could not predict the future pricing behaviour of its competitors. Allergan failed to see how a campaign based on pure speculation and not fact could possibly be acceptable under the Code. Any cost saving claims so formulated were highly likely to be inaccurate. When extrapolated over a long time period, they became increasingly unsupportable and misleading whilst artificially inflating the potential savings to a primary care trust (PCT). Allergan thus alleged that the budget impact model and any materials associated with it were in breach of Clauses 7.2 and 7.3 of the Code.

Allergan also had major concerns about the following statement (or similar) which had featured prominently on all campaign materials, including the budget impact model and advertisement at issue:

> 'The current assumption is that Xalatan and Xalacom will come off patent in the UK in July 2011. However, a paediatric development programme is ongoing in Europe which, if all the requirements of the EU Paediatric Medicines Regulation are met, may result in an extension of 6 months.'

Allergan believed this statement was teaser

advertising intended to elicit interest in this area and also promotion of a medicine outside the terms of its marketing authorization. Allergan alleged that the budget impact model and advertisement were in breach of Clauses 3.2, 9.1 and 9.2.

Allergan understood that representatives used the budget impact model at issue to demonstrate potential five-year cost savings to health professionals. Allergan understood from its discussion with Pfizer that the model itself was not left with customers. However, the 'print' and 'save' functions within the model implied that the information and potential outputs from the model could be left with the customer to share with colleagues.

The model compared acquisition costs for the four first-line prostaglandin monotherapies: Xalatan (latanoprost), Lumigan (bimatoprost), Travatan (travoprost) and Saflutan (tafluprost); and the three second-line prostaglandin combination therapies: Xalacom (latanoprost plus timolol), DuoTrav (travoprost plus timolol) and Ganfort (bimatoprost plus timolol).

The model itself, relatively simple in design, was based entirely on predicted medicine costs which were then used to calculate savings for any given PCT population. It did not take into account other aspects of glaucoma treatment which might impact cost savings, for example additional therapy which might be required in addition to the chosen medicine and additional clinic visits.

Allergan did not consider that the statements at the beginning of the model to acknowledge the inability to accurately predict future prices of medicines and to put the responsibility on the customer for any data entered, made the principle of the model acceptable.

Allergan alleged that Pfizer's statements that '… NHS staff are aware of changes in drug costs and are able to reach their own conclusions on pricing changes ...' and that '… the model allows a simple way of exploring potential cost changes with the impact of loss of exclusivity, and will be based on the clinician's own opinion…' was disingenuous. The major driving factor of the model outcomes was the predicted estimate of the price of generic Xalatan/Xalacom and its competitors. This required an adequate understanding of pricing behaviour in the market following loss of patent to make the estimate accurate and valid. Allergan considered that in the majority of cases, this would inevitably be representative-led due to the likely minimal knowledge of health professionals in this area.

If the customer was unsure as to what figures to input, Allergan understood that the representatives had been briefed as to appropriate suggestions that might be made. Allergan was concerned about the nature of this guidance, which was based on IMS research conducted for Pfizer in January 2008.

Pfizer had stated that '…the IMS data used as a basis for discussion on pricing post loss of exclusivity are real life data for a range of products that have lost exclusivity in the recent past …'. Allergan considered that there were several weaknesses to this data and hence any conclusions based upon this material. Aside from the overriding fact that the data entered remained a theoretical estimate, these concerns included:

- The products chosen by IMS for analysis. In Allergan's opinion, determining comparators for analogue modelling was subjective depending on the screening questions to access the respective markets. Allergan considered that the six products chosen for the Pfizer model were not truly representative of, or relevant to, the glaucoma market. For example it was very difficult to draw conclusions from the hypertensive market to the glaucoma market given such different dynamics. Considering that predictions of the likely pricing behaviour of Xalatan/Xalacom generics were based on what Allergan believed were unrepresentative analogues for modelling, it was concerned that the cost-saving calculations subsequently formulated would be misleading.
- The simplistic nature of the research. This focused only on the impact of a lead brand loss of product patent and did not consider the impact on the second or third brand from the loss of a lead brand patent, such as that of the impact of latanoprost loss of patent on travoprost or bimatoprost.
- The failure to consider the loss of patent of subsequent brands, such as that of travoprost in 2014, which was within the scope of the model's projected five-year calculations.
- The nature of the briefing given to representatives as to what data to enter into the model. Allergan had doubts as to whether the price selected for input would be fair and reflect the gradually declining prices as suggested by the research. In this regard Allergan noted that it had received reports from some of its customers that Pfizer representatives had referred to the lowest prices quoted within the IMS data.

The following statement had been included in all campaign materials that Allergan was aware of to date, including the current budget impact model:

'... The current assumption is that Xalatan and Xalacom will come off patent in the UK in July 2011. However, a paediatric development programme is ongoing in Europe which, if all the requirements of the EU Paediatric Medicines Regulation are met, may result in an extension of 6 months…'.

Allergan strongly disagreed with Pfizer's opinion that to not include the above statement in materials would be misleading. Similarly Allergan did not agree with Pfizer's previous assertions that it was only '…a brief factual statement' that was not promotional and '…has been included for complete transparency…'. Allergan submitted this was an opportunity to elicit interest and promote a

potential new indication outside of the terms of the current marketing authorization.

Allergan noted that the advertisement at issue (ref XT1583c) urged health professionals to initiate patients on Xalatan or Xalacom now to have the prospect of realising 'significant long-term savings when generic versions became available …'. No specific mention was made of the budget impact model in this advertisement. However, one would assume that this would be offered for discussion should the reader decide to 'find out more', as directed in the advertisement. For all the reasons stated previously, Allergan believed the significant savings to which Pfizer alluded were based purely on speculation not fact and were thus unacceptable under the Code.

In summary, Allergan alleged that the materials and associated activities outlined above were in breach of the Code. It failed to see how a campaign based on pure speculation and not fact could possibly be acceptable under the Code. Any cost saving claims so formulated were highly likely to be inaccurate. When extrapolated over a long time period, they became increasingly unsupportable and misleading whilst artificially inflating the potential savings to a PCT. Therefore, in Allergan's view the model and any materials associated with it were in breach of Clauses 7.2 and 7.3.

RESPONSE

Pfizer stated that it was committed to building and establishing trust between itself and the UK healthcare system. The UK environment was now such that many customers, whether they were payers or prescribers, valued a conversation with the pharmaceutical industry about the current and future cost of medicines. Pfizer strongly believed that these conversations allowed it to engage and collaborate in a more transparent way, thereby creating openness and integrity.

Pfizer noted that the budget impact model and advertisement covered the loss of exclusivity of its medicines Xalatan (latanoprost) and Xalacom (latanoprost plus timolol), which would be the first of the prostaglandin-based treatments for glaucoma to lose exclusivity in 2011. Allergan had alleged that the model made unreasonable and speculative claims, and did not take into account loss of exclusivity of competitor brands.

The NHS was very alert to cost of treatments and the UK had one of the highest usage of generic medicines. The increased focus on NHS budgets, exacerbated by the current financial climate, had accentuated the focus of prescribers and payers on the cost of treatment and had made prescribers increasingly accountable for their medicine budgets.

Prescribers, budget holders and medicines managers were responsible for forecasting costs and must anticipate potential cost savings from the availability of generic medicines following loss of exclusivity of a major brand. The budget impact model had therefore met with great interest from prescribers and budget holders as the information which it provided could demonstrate how cost savings might be realised.

The model allowed customers to model potential cost savings over a five year period by comparing the prescribing costs of Xalatan or Xalacom with that of competitor products taking into account the dates of loss of exclusivity. The figures calculated in the model were in the first instance based on the current NHS prices of medicines updated monthly from MIMS. The model allowed customers to input their own data which might differ from NHS prices. Customers could use their experience to estimate prices they were likely to pay following loss of exclusivity. This could be supported by evidence from reviewing price reductions for six major products before and after they lost exclusivity using IMS data. The price of Xalatan or Xalacom and their competitors could be independently altered depending on the customer's wishes. Contrary to Allergan's claims, the model could be modified to take into account dates of the competitors' loss of exclusivity. The model offered a dynamic assessment of projected costs in the future.

Although any form of forecasting was inexact, this method allowed customers to model a number of different scenarios and observe the effect on their budget. In addition, and in the interests of transparency, the model could be printed or saved and a record left with the customer. The budget impact model made no quantitative claims around future cost savings or efficacy of medicines. Pfizer believed therefore that the budget impact model was not in breach of Clauses 7.2 or 7.3.

The associated advertisement highlighted to prescribers and budget holders that Pfizer's medicines would be the first of the topical prostaglandins to lose exclusivity. Pfizer did not consider that the claim in the advertisement, 'significant cost savings are in sight' was misleading as major brands in the UK losing exclusivity tended to experience rapid generic competition as evidenced by the IMS data. Optimal prescribing considered the needs of the patient, the prescriber and the budget holder, namely efficacy, tolerability, adherence and price. Therefore Pfizer did not believe the advertisement was in breach of Clauses 7.2 or 7.3.

Pfizer submitted that it had now completed a paediatric investigation plan the results of which were currently being evaluated by the European Medicines Agency. If Pfizer successfully completed the regulatory process, it intended to apply for the six month extension to the supplementary protection certificate for latanoprost in eligible EU countries (including the UK) in accordance with the EU Paediatric Regulation. Although the paediatric investigation plan was not complete when the budget impact model and advertisement were launched, Pfizer considered that it would be misleading not to disclose the significant possibility

of this exclusivity extension to customers, given the context and purpose of the budget impact model. In the interest of transparency, Pfizer therefore included a statement explaining the current situation on all material relating to the issue of loss of exclusivity. As this statement was clear and not misleading Pfizer did not consider that it was advertising as described in the supplementary information to Clauses 9.1 and 9.2. The arguments around cost savings still held with a six month exclusivity extension, as the loss of exclusivity date would still be significantly earlier than that of any of the competitors. There was the facility to model either date in the budget impact model. Pfizer's representatives had been clearly briefed that its products were not yet licensed for paediatric use and so Pfizer refuted that it had tried to promote its products before marketing authorization. Pfizer did not believe the inclusion of a statement regarding potential changes in loss of exclusivity date breached Clauses 3.2, 9.1 and 9.2.

In summary, the budget impact model was an innovative method to help NHS prescribers and budget holders make informed decisions on comparative five year prescribing costs based on evidence of previous experience in price falls after loss of exclusivity. All prices in the model were checked monthly and revised accordingly.

In response to a request for further information Pfizer provided a copy of the briefing material for the original Budget Impact Model and customer letters. The updated briefing material highlighting the most recent changes had already been provided. The customer letters were not used with the current version of the budget model as a disclaimer screen had now been incorporated into the model itself.

In response to a further request for further information, Pfizer referred to the lack of initial savings demonstrated with Xalatan or Xalacom and stated that initiating patients on the less expensive medicines might be cheaper in the short term, but the budget impact model sought to demonstrate that savings over the longer term (five years) could be achieved with the advent of loss of exclusivity and inevitable fall in price of Xalatan and Xalacom. The print-out provided to the Authority showed the framework of the model. The data boxes were not populated at the start but became populated as the representative's interaction with the health profession progressed. It was difficult to illustrate this dynamic process on paper.

Pfizer stated that the model explored possible five-year cost savings with reference to the date of loss of exclusivity of Xalatan and Xalacom, due to occur at either July 2011 or January 2012. The choice of loss of exclusivity date lay with the health professional. Once the date was selected the module calculated price after loss of exclusivity by applying a percentage reduction to the price of Xalatan or Xalacom in the appropriate box in the price modulation table. The scenarios discussed between representative and the health professional were not fixed but were open to variation and formed the basis for their discussion.

In summary, whilst initially current prices of Xalatan and Xalacom might be higher than competitors, the model might demonstrate cost savings over a five year period due to loss of exclusivity.

PANEL RULING

The Panel noted Pfizer's submission that many of its customers valued a conversation with the pharmaceutical industry about the current and future cost of medicine. The Panel accepted that that might well be so but nonetheless any activity in this regard had to comply with the Code. The Panel noted that the advertisement at issue promoted Xalatan and Xalacom as did the budget impact model. The requirements of the Code with regard to the promotion of medicines thus applied.

The advertisement at issue was headed 'Is your prescribing optimised?' below which it stated 'Xalatan and Xalacom will be the first prostaglandins to come off patent'. Readers were told that initiating patients on Xalatan or Xalacom now meant that they had the prospect of realising significant long-term savings when generic versions became available without having to interrupt patient treatment. Readers were invited to find out more by telephoning a free-phone number or by contacting an email address. Xalacom and Xalatan were currently more expensive than some of the competitor products and thus initiating patients now on Pfizer's products might mean more expensive treatment costs until July 2011 or January 2012 whenever the products came off patent. It was of course likely that savings would be made once generic versions were available. A footnote explained that the current assumption was that Xalatan and Xalacom would come of patent in July 2011. However, a paediatric development programme was ongoing in Europe, which, if all the requirements of the EU Paediatric Medicines Regulations were met, might result in an extension of 6 months. The Panel thus noted that Xalatan and Xalacom might not come off patent until January 2012 ie almost two years after the advertisement was prepared. In that regard the Panel questioned the use of the claim 'Significant savings are in sight'.

The Panel noted that both the advertisement and the budget impact model which clearly promoted Xalatan and Xalacom, referred to the paediatric development programme. The Xalatan summary of product characteristics (SPC), however, stated that safety and effectiveness in children had not been established. Xalatan was therefore not recommended for use in children. The Panel considered that it was important to give an idea of time scale regarding when the products would come off patent however there was no need to explain the reason why. The Panel considered that the advertisement and the budget impact model insomuch as they also referred to the ongoing paediatric development programme, were

inconsistent with the particulars listed in the Xalatan and Xalacom SPCs. A breach of Clause 3.2 was ruled. The Panel further considered that such promotion of a medicine meant that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel did not consider that the statement regarding the paediatric development programme constituted 'teaser' advertising which was material issued to elicit interest in something which would follow at a later date without providing any information about it. Information about Xalatan and Xalacom had been provided. No breach of Clauses 9.1 and 9.2 was ruled in this regard.

The Panel noted that the five year budget impact model compared the acquisition costs of Xalatan and Xalacom with that of its competitors and explored possible five-year cost savings that might be achieved when Xalatan and Xalacom came off patent. In that regard the Panel considered that the impact model promoted Xalatan and Xalacom and made comparative claims vs their competitors. The users of the model were informed that: 'The predicted dates for loss of exclusivity (LOE) for [the products featured] are estimates based on current understanding. Please be aware that it is not possible to accurately predict the price of Xalatan, Xalacom, Lumigan, Travatan, Saflutan, Duo Trav and Ganfort post-LOE. The predicted prices will be estimates based on your current understanding, therefore all post LOE prices used in the model are assumptions as selected by you. All analyses within the model that incorporate LOE are therefore also assumptions and may not provide an accurate reflection of the value of Xalatan and Xalacom in the future'.

The Panel noted that having discussed the budget impact model with a representative, a health professional was required to sign a letter accepting the above. The letter also referred to the provision of print outs.

The Panel noted from the representatives' briefing material that the monthly price for a competitor product could not be altered within the five year projected period. The percentage reduction in price for a product was to be based on discussions with the NHS customer.

The Panel noted that by their nature, financial models such as that at issue could only give estimates and that the audience would understand such constraints. The question was whether such estimates were reasonable. The Panel considered that while it might be acceptable for a company to present short-term budget models about its own medicines, over which it could be assumed to have reasonable control, to present a long-term model which generated comparative claims vs competitor products introduced many uncertainties. The model at issue covered five years; the date of the loss of patent for Xalatan and Xalacom was dependent upon the outcome of an ongoing paediatric development programme. The model could be modified to take account that Travatan was expected to come off patent within five years; the price of generic versions of Xalatan and Xalacom were decided upon by the health professional. Pfizer could not accurately predict competitors' pricing strategies as the dynamics of the market changed. Nor could Pfizer accurately predict government strategy as noted in the model itself, 'Product prices are correct based on the current situation. However prices are subject to change and may go up or down as a result of UK PPRS requirements'. The fact that in the short-term, depending on the date of loss of exclusivity, it would be more expensive to initiate patients on Xalacom and Xalatan than some of the competitors had not been made clear.

Overall, the Panel considered that the budget impact model was based on too many assumptions and uncertainties such that the comparative data generated was too speculative and in that regard it was misleading. The Panel ruled breaches of Clauses 7.2 and 7.3 as alleged. The Panel considered that its comments about the budget impact model were relevant in relation to the cost savings claims such as 'significant saving are in sight' in the advertisement and similarly ruled breaches of Clauses 7.2 and 7.3 as alleged.

Complaint received **28 April 2010**

Case completed **26 July 2010**

GENERAL PRACTITIONER v ASTRAZENECA

Conduct of representative

A general practitioner complained to AstraZeneca about the conduct of one of its representatives and copied his letter to the Authority.

The complainant noted that he had met the representative one afternoon shortly before the start of a busy surgery. Unfortunately the meeting was arranged without his prior knowledge or consent and in that regard he considered it an unsolicited visit.

The representative (whom the complainant had not met before) began by stating that the practice nurses had recently told her that '[The complainant] did not seem to know a lot about Symbicort Smart and had been prescribing Salbutamol to patients and so could she (the representative) "have a word" with [the complainant]!'.

The complainant immediately expressed his surprise and disbelief that one of his nurses had said this to an outsider rather than discussing the matter with him first and, indeed, at an appropriate forum. The complainant repeatedly asked the representative if this was indeed what the nurse(s) had said and she replied that it was at least three times and even described the nurse but refused to name her.

The complainant stated that despite realising that he was upset by her comments, the representative continued to speak in a patronising and condescending manner without trying to establish the facts or ascertaining his prior knowledge on the subject.

The representative did not introduce the topic of SMART dosing in the context of asthma management and came across as unilaterally and blatantly trying to 'sell a product' without any due comparison or justification. In order to avoid feeding her incorrect assumption, the complainant illustrated his more than adequate knowledge on the subject.

The meeting closed amicably (given the circumstances) and the complainant stated that he would look into this matter further as there were several areas of concern.

The complainant submitted that he and his practice manager had interviewed the practice nurses individually; all of them denied making or implying any of the above statements or remarks. Furthermore, there were no examples or concerns expressed regarding SMART prescribing.

It thus appeared that the representative had been dishonest and made false representations during her meeting with the complainant to suit her (and possibly AstraZeneca's) gains. The representative's attitude was insensitive, unprofessional and irresponsible and did not befit an AstraZeneca representative and brought the company into disrepute and breached the Code on several counts.

The complainant requested a detailed inquiry from AstraZeneca, with a view to appropriate reprimand, sanctions and reassurances. In almost 20 years as a doctor, this was his first unsavoury encounter with a representative!

The complainant was also concerned about the way in which the matter had been handled. Initially it appeared that the representative would issue a full written apology and meet the complainant to try and resolve this matter. Shortly afterwards, the practice manager was informed that the complainant needed to write to corporate governance at AstraZeneca via the representative; this course of action was strange and unacceptable.

The area manager informed the practice manager of the complicated governance process that had to be followed. The complainant was assured of feedback following the area manager's meeting with the representative. However this had not happened.

The complainant expected a detailed report from AstraZeneca including remedial suggestions to prevent a recurrence. Whilst this matter was unresolved, AstraZeneca was asked not to engage with the practice.

Furthermore, all pharmaceutical representatives had clear instructions not to liaise/interact directly with practice nurses during practice hours as the practice had a designated forum for such meetings and would ask that AstraZeneca adhered to that policy; the representative at issue had thus also breached this policy.

Clearly, the representative would not be welcome at the practice in the future.

AstraZeneca's response was sent to the complainant and his further comments invited. The complainant stated that on the whole he found AstraZeneca's response totally unsatisfactory. Details were provided.

The detailed response from AstraZeneca is given below.

The Panel noted its role was to determine whether or not there had been a breach of the Code. As

acknowledged by the complainant some of his concerns were not matters within the scope of the Code.

The Panel noted that the parties' accounts differed markedly. It was difficult in such circumstances to determine where the truth lay. The Panel noted that it was for the complainant to establish his case on the balance of probabilities.

The complainant alleged that the representative had explained that a practice nurse had stated that the complainant did not know a lot about Symbicort SMART and suggested that the representative have a word with the complainant. This was denied by AstraZeneca which stated that on arrival at the GP practice a practice nurse gestured the representative and her line manager to come into her office. They were not made aware of any practice policy regarding such calls. According to the representative and her line manager this nurse suggested they see the complainant to discuss the use of Symbicort SMART in asthma patients including concomitant use of the blue inhaler. The complainant stated that all of his practice nurses denied making such comments. The Panel also noted the complainant's allegation that the representative's attitude during the interview was insensitive and unprofessional and that the promotion was without due comparison or justification. This was denied by AstraZeneca which referred to the contemporaneous note of its representative. The representative in question had not been at work and AstraZeneca had been unable to comment on the complainant's further information. The complainant provided a very full account of the interview. It was clear that the complainant had been upset. Representatives' calls should not cause inconvenience to those upon whom they call.

The Panel decided that it was not possible to determine on the balance of probabilities precisely what had occurred. The Panel noted that extreme dissatisfaction must be present on the part of a complainant before he/she was moved to submit a complaint. Nonetheless, taking all the evidence into account the Panel decided that it was not possible to determine precisely what had occurred and thus ruled no breach of the Code.

A general practitioner complained to AstraZeneca UK Limited about the conduct of one of its representatives and copied his letter to the Authority.

COMPLAINT

The complainant noted that he had met the representative one afternoon of 9 February, shortly before the start of a busy surgery. Unfortunately the meeting was arranged without his prior knowledge or consent and in that regard he considered it an unsolicited visit.

Rather than attempt to establish any kind of rapport with the complainant, the representative (whom the complainant had not met before) opened her conversation by stating that at a recent meeting with the practice nurses she had been told that '[The complainant] did not seem to know a lot about Symbicort Smart and had been prescribing Salbutamol to patients and so could she (the representative) "have a word" with [the complainant]!'.

The complainant immediately expressed his surprise and disbelief that such a statement had been made by one of his nurses to an outside party rather than discussing the matter with him first and, indeed, at an appropriate forum. The complainant repeatedly asked the representative if this was indeed what the nurse(s) had said and she replied that it was at least three times and even described the nurse as 'short, fair and blonde' but refused to name her claiming that she was not aware of it.

The complainant stated that despite realising that he was upset by her comments, the representative continued to speak in a patronising and condescending manner without trying to establish the facts or ascertaining his prior knowledge on the subject.

The representative did not introduce the topic of SMART dosing in the context of asthma management and came across as unilaterally and blatantly trying to 'sell a product' without any due comparison or justification. In order to avoid feeding her incorrect assumption, the complainant illustrated his knowledge on the subject and it was apparent to the representative that this was sufficiently more than adequate as she later admitted.

The meeting closed amicably (given the circumstances) and the complainant stated that he would look into this matter further as there were obviously several areas of concern.

The complainant submitted that he and his practice manager had investigated this matter thoroughly and had interviewed the practice nurses individually; all of them denied making or implying any of the above statements or remarks. Furthermore, there were no examples or concerns expressed regarding SMART prescribing or indeed management of asthma patients as a whole.

It thus appeared that the representative had been dishonest and made false representations during her meeting with the complainant to suit her (and possibly AstraZeneca's) gains and this was a serious misdemeanour and of concern.

The complainant alleged that the representative's attitude was insensitive, unprofessional and irresponsible and did not befit an AstraZeneca representative and brought the company into disrepute not to mention breaching the Code on several counts.

The complainant requested a detailed inquiry from AstraZeneca into this matter with a view to

appropriate reprimand and sanctions against the representative and he also sought reassurances that this behaviour would never be repeated. In almost 20 years as a doctor, this was the complainant's first unsavoury encounter with a pharmaceutical representative!

The complainant was also concerned about the manner in which the episode had been handled so far. The practice manager was initially informed that the representative was prepared to issue a full written apology and meet the complainant to try and resolve this matter. Shortly afterwards, the practice manager was informed that the complainant needed to write to corporate governance at AstraZeneca but send the letter to the representative's home address which was strange and unacceptable.

The practice manager was then contacted by an area manager who informed the complainant of the complicated governance process that had to be followed. The complainant was assured of feedback following the area manager's pre-arranged meeting with the representative. However this had not happened.

The complainant expected a detailed report from AstraZeneca including remedial suggestions to prevent a recurrence. The complainant further asked that, whilst this matter was unresolved, AstraZeneca refrained from engaging with the practice until professional trust was restored.

Furthermore, all pharmaceutical representatives had clear instructions not to liaise/interact directly with practice nurses during practice hours as the practice had a designated forum for such meetings and would ask that AstraZeneca adhered to that policy too which, again, the representative at issue had breached as well.

Clearly, the representative would not be welcome at the practice in the future.

When writing to AstraZeneca the Authority asked it to respond in relation to Clause 2, 7.2, 8.2, and 15.2 of the Code.

RESPONSE

AstraZeneca explained that 'Symbicort SMART' was a company trademark and represented **S**ymbicort **M**aintenance **A**nd **R**eliever **T**herapy which was a licensed treatment approach for Symbicort, for it to be taken as regular maintenance treatment and as needed in response to asthma symptoms. The SMART licence was available for the 100mcg/6mcg and 200mcg/6mcg presentations of Symbicort but not the 400mcg/12mcg presentation.

AstraZeneca explained that on 4 February, the representative and her manager visited the complainant's practice to ask for an appointment with one of the practice nurses (an unsolicited call). When they arrived at reception, and before they had asked for the appointment, the nurse spotted them and gestured to them to go to her which they did; they were not aware of any specific policy in this practice about calls/interactions with practice nurses and nor were they informed of such a policy by the nurse. During this interaction (attended by both the representative and her manager) they discussed an upcoming AstraZeneca educational meeting. The representative and her manager also understood from the practice nurse that they should arrange to see the complainant to discuss Symbicort SMART and its licensed use in asthma patients, including those who were also concomitantly taking blue inhalers. The nurse asked them to 'have a word' with the doctor about this topic. The representative was told that the best way to arrange an appointment was via the practice manager.

The representative then asked the practice manager for an appointment with the complainant. When asked if this was important the representative said that it was in the belief that the appointment had been recommended by one of the practice nurses. The practice manager duly arranged an appointment. The representative assumed that the practice manager had the authority to arrange such an appointment; she was not told otherwise. AstraZeneca noted that the meeting with the complainant was on 10 February.

The representative's record of the meeting with the practice manager stated 'Agreed to arrange an appointment with [the complainant] to discuss SMART management'. The contemporaneous call record entered by the representative indicated that the 'Desired Customer Action' for this appointment (as desired by the representative) was 'To ensure that he is aware of the correct license indication and understand target pts and how to rx'. This was not inconsistent with the reasons that the representative and manager believed they were recommended to see the doctor by the nurse.

Based on this information, AstraZeneca believed that the representative acted in good faith upon the recommendation of a practice nurse to call on the complainant to discuss Symbicort SMART and that the appointment was arranged via an appropriately authorized practice official. AstraZeneca thus denied a breach of Clause 15.2.

AstraZeneca noted that the complainant appeared to allege that information, claims or comparisons provided verbally by the representative regarding Symbicort SMART were not balanced/objective and/or were exaggerated or had undue emphasis ('[she] came across as unilaterally and blatantly trying to 'sell a product' without any due comparison or justification'). The complainant had not referred to any specific promotional claims or materials.

In responding to this point, AstraZeneca relied on the contemporaneous written call record entered by the representative and the prior information supplied by her. The call record indicated that the appointment with the doctor took place at 16:30 on 10 February.

The representative recollected that during this call she initiated a discussion of Symbicort SMART specifically in relation to the management of patients with asthma, including those who were also taking blue inhalers. They discussed how the SMART licence changed the practice of prescribing blue inhalers.

AstraZeneca noted the 'Agreed Customer Action' was 'Understands and will use a blue inhaler in pt if he feels the needs and said that SMART was not the only indication for Symbicort'. This was not inconsistent with the representative's recollection of the clinical discussion about Symbicort SMART, as outlined above.

The representative also recollected a brief discussion about exercise-induced asthma and that this did not fall into the SMART licence indication (the summaries of product characteristics (SPCs) for the SMART licence doses stated that 'the prophylactic use of Symbicort, eg. before exercise, has not been studied' and that therefore reliever inhalations of Symbicort were not intended for such use).

There was also a brief discussion of the British Thoracic Society (BTS) Guidelines on the management of asthma; a promotional leavepiece on the place of Symbicort SMART in the BTS guidelines was left with the complainant. The leavepiece gave a summary rationale/justification for the use of Symbicort in asthma on the basis that it was included in BTS clinical guidelines.

AstraZeneca noted that the representative was unavailable to respond to the specific point in the complainant's letter that 'She did not try and introduce the topic of SMART dosing in the context of asthma management ...'. However, in the prior information submitted by the representative, there was no indication of a specific discussion regarding doses or concerns expressed regarding a lack of such a discussion.

Based on this information, AstraZeneca could not establish evidence that the representative promoted Symbicort '… without any due comparison or justification'. The company therefore denied a breach of Clause 7.2.

AstraZeneca noted the allegation that the representative spoke to the complainant ' in a patronizing and condescending manner …' and considered that, in relation to the Code, this was an allegation that the representative disparaged the clinical or scientific opinion of a health professional.

AstraZeneca submitted that the representative recollected that the complainant was offended by the reason given by her for the call, ie that she had been recommended by one of the practice nurses to discuss Symbicort SMART and its licensed use in asthma patients, including those patients who were also concomitantly taking blue inhalers. The representative explained that she was merely following up on this recommendation.

The rest of the call focused mainly on a clinical discussion of Symbicort SMART and its use in patients with asthma including those also taking the blue inhaler. The representative agreed that it was appropriate for the complainant to continue prescribing Symbicort SMART as he had been, in line with his clinical judgement. This was reflected in the representative's call notes which stated 'Understands and will use a blue inhaler in pt if he feels the needs and said that SMART was not the only indication for Symbicort'.

The representative recalled that towards the end of the call the complainant was not as upset as he had been at the beginning. AstraZeneca noted the complainant's submission that 'The meeting closed amicably (given the circumstances) ...'.

Based on this information, AstraZeneca could not establish that the representative had disparaged the clinical or scientific opinion of a health professional. Therefore the company denied a breach of Clause 8.2.

AstraZeneca noted that the complainant was concerned about the manner in which the episode had been handled and considered that, in relation to the Code, this was an allegation that the representative and/or the manager had not maintained a high standard of ethical conduct.

AstraZeneca submitted that during and after the call, the representative recognized that the complainant was upset as stated in the call record, 'He was not happy that I had an appointment'. However, as detailed above, the representative judged that the ambience had improved in the latter part of the call.

The following week, the practice manager told the representative that the complainant was concerned about the way in which the appointment had been arranged and required an apology. The representative discussed this with her manager and was instructed to clarify the specific concerns before responding. In the subsequent discussion with the practice manager, the representative was informed that the complainant required a written apology.

The representative undertook to write an apology to the complainant in response to any letter of complaint from the complainant setting out the specific concerns and that this letter could be sent to the representative's home address.

However, in a telephone conversation with him on 18 March, the area manager told the complainant that any letter of apology from the representative would require AstraZeneca Head Office approval, and as a first step in the process of addressing his concerns, the manager asked the complainant to submit a written statement setting out the specific points of concern. The complainant declined to do this and requested that the representative write a statement first setting out the issues, since she should already know what they were, and respond

to them accordingly in an honest manner.

The area manager subsequently requested the compliance department at AstraZeneca to further follow up this matter. The compliance department duly telephoned the practice to request a clarification of the concerns verbally but was unsuccessful and therefore wrote to the complainant requesting this on 26 March and then in a follow up letter on 29 April.

AstraZeneca accepted that although the representative (in good will) initially promised, but did not write, a letter of apology, it was appropriate for the manager to first ask for a written clarification of the specific concerns before responding in writing.

Given the above, AstraZeneca believed that overall a reasonable effort was made to clarify and respond to specific concerns and it denied a breach of Clause 15.2.

AstraZeneca fully accepted that the complainant had a poor opinion of the company. However, as detailed above the company did not believe there had been breaches of the relevant clauses of the Code, or that the circumstances were such as to bring discredit upon, or reduce confidence in the pharmaceutical industry. AstraZeneca thus denied a breach of Clause 2.

FURTHER COMMENTS FROM THE COMPLAINANT

AstraZeneca's response was sent to the complainant for comment. The complainant stated that on the whole he found AstraZeneca's response totally unsatisfactory. He started with some general comments:

- The complainant was disappointed that AstraZeneca's head of compliance had chosen to only write to the Authority as his letter of complaint was addressed directly to AstraZeneca's compliance leader and the complainant would therefore have expected him to respond to him out of professional courtesy.
- The complainant saw no expression of remorse at all in the letter which seemed to focus more on defending the possible breaches of the Code rather than dealing with specific issues raised.
- The complainant found it hard to understand why AstraZeneca had not consulted with/obtained a statement from its representative before responding to the complaint and relied on antiquated information which it claimed to be contemporaneous. Indeed, if the representative did make such extensive notes; then this surely must be because she realised she had done something 'wrong'.
- The complainant queried why the representative was 'unavailable' unless this was again a demonstration of how lightly AstraZeneca regarded this issue.
- The complainant had not come across any mention of an apology which he would most certainly still expect from the representative.

More specifically; the complainant had the following to add to enable the Authority to make its rulings:

- The response letter made frequent reference to the fact that the representative had acted on the recommendation of one of the practice nurses. Investigations so far had revealed this to be untrue and the complainant had no option but to ask the AstraZeneca representative to identify the nurse as all of the complainant's nurses interviewed denied making the condescending comment mentioned to the complainant by the representative and also clearly stated that they did not have any issues with the complainant's prescribing methodology (SMART or otherwise).
- Further to the complainant's discussions with his practice manager, she recalled that the reason given by the representative to meet with him specifically was because she had missed the complainant at her promotional meeting with the other GPs and not that she was acting on the behest of a nurse (yet another example of misrepresentation).
- The complainant found the head of compliance's description of the actual interaction inaccurate and extremely defensive.
- The complainant did not think there could be anything more disparaging than a pharmaceutical representative telling an experienced doctor she had not met before that '… you don't seem to know a lot about SMART prescribing and I have been asked to have a word with you'!
- The complainant would not expect any pharmaceutical representative to base their interaction with a health professional on an assumption or alleged comment from a nurse and then proceed to talk down to that person even after realising that their behaviour had upset them! This was what had caused the complainant the most distress and as he had pointed out earlier; he did not see an apology forthcoming at all.
- The response letter seemed to describe an interactive discussion around Symbicort SMART. The complainant told the Authority that he had no option but to quickly correct the representative's misplaced preconceptions and delivered a succinct summary on asthma management and the place of the SMART regime to demonstrate convincingly his grasp and command on the subject following which she conceded: 'I don't really need to tell you anything!'.
- The complainant had to take control and close the meeting amicably (this was what sensible well-trained professionals did in such situations) in order to compose himself before his afternoon surgery as the representative's demeanour did not change even as she realised she had acted wrongly. She casually stated to the complainant

shortly before she left '… I hope this isn't a problem. I didn't mean to cause any trouble …'. Did the Authority need any more proof of her admission of misbehaviour?

- There was further falsification about the sequence of events. The complainant had confirmed the facts yet again with his practice manager who could confirm that further to her discussions with the AstraZeneca representative, the representative actually agreed to submit an apology to him (either written or face-to-face). This was prior to the manager getting involved.
- The complainant stated that the AstraZeneca manager seemed intent on going down a formal complaints process and the complainant explained that this was unnecessary as the representative had already agreed to a written apology (and thereby admitting her misdemeanour). For this reason the complainant declined to provide a formal statement and suggested that the manager meet with the representative to ascertain the facts and arrange for an apology. The complainant noted that he had given AstraZeneca a written statement but that the company had still not apologized to him.
- The AstraZeneca manager clearly stated that she would meet the representative the following week and would contact the complainant further to this. (Which she never did and instead the practice received a call from the Compliance Leader and then a letter to which the complainant had obviously responded.)

The complainant reiterated his deep dismay at the total lack of any genuine repentance in the response from AstraZeneca which was unfortunately cluttered with the sort of corporate deniability one would not normally expect from such a company; which appeared to have covered up its representative's unprofessionalism in order to deflect any criticism and penalties from itself.

Sadly the complainant now had an even poorer opinion of the company and its representative. The complainant had hoped that by addressing his concerns appropriately, AstraZeneca could have tried to repair the damage caused to its relationship with the practice which now seemed irreparable and he again asked the company not to interact with the practice (or its employees during usual working hours) whilst this matter remained unresolved and until faith was restored.

The complainant would, of course, respect any rulings made by the Authority with regard to any likely breaches of the Code; but, as stated earlier, his concerns were much more than just this and AstraZeneca had failed to deal with these honestly and completely to his satisfaction.

FURTHER COMMENTS FROM ASTRAZENECA

The complainant's additional comments were provided to AstraZeneca.

AstraZeneca stated that its response above relied on information supplied by the representative in March when her manager was initially investigating this issue and additionally on call notes recorded in the territory management system. AstraZeneca had not been able to obtain a statement from the representative due to long term absence. This was not, in any way, an indication that AstraZeneca regarded this issue lightly.

AstraZeneca representatives were required to maintain contemporaneous notes in relation to calls they made on health professionals and the notes generated by the representative in this case were in keeping with that requirement and were not 'extensive' as suggested. There was no evidence to suggest that they had been generated because the representative realised she had done something wrong.

In relation to the complainant's specific points AstraZeneca had the following comments.

From the complainant's initial letter, AstraZeneca noted that he had already interviewed the relevant practice staff. Therefore AstraZeneca did not attempt to repeat such interviews and relied solely on the submissions of the AstraZeneca staff. AstraZeneca therefore did not have any direct information from named practice staff to submit.

The line manager's recollection was that the grounds given for booking the appointment with the practice manager were that a practice nurse had asked them to go and see the complainant regarding Symbicort and its licensed use in asthma patients, including those patients who were also concomitantly taking blue inhalers. They recalled that the nurse asked them to 'have a word' with the doctor in relation to this topic and not because the representative had missed the complainant at a promotional meeting.

From the complainant's initial letter the representative explained the reason for the call. The letter stated that the representative '…opened her conversation by stating that at a recent meeting with my practice nurses, she had been told that [the complainant] did not seem to know a lot about Symbicort Smart and had been prescribing Salbutamol to patients and so could she have a word with me'. This was consistent with the representative's account of events. However, in the latest correspondence the complainant suggested that the representative had initiated this remark with no context or reason for the call by saying '…you don't seem to know a lot about SMART prescribing and I have been asked to have a word with you'. This appeared to differ from the specific wording for this opening line originally given by the complainant and the account given by the representative. Within the context of the complainant's originally stated reasons given to him by the representative for making the appointment it did not appear that it was the intention of the representative to be disparaging.

The prior information from the representative was

that the call focused mainly on a clinical discussion of Symbicort SMART and its use in patients with asthma including those also taking the blue inhaler. The representative agreed with the patient that it was indeed appropriate for the doctor to continue prescribing Symbicort SMART, as he had been, in line with his clinical judgement. This was reflected in the representative's call notes which stated 'Understands and will use a blue inhaler in pt if he feels the need and said that SMART was not the only indication for Symbicort'. As the discussion progressed the representative recalled that towards the latter part of the call the doctor was not as upset as he had been at the beginning. AstraZeneca noted in the doctor's letter of complaint that 'The meeting was closed amicably (given the circumstances)…'.

Since the representative had been unavailable since receipt of the formal complaint, AstraZeneca was not able to confirm with her whether she made certain statements during the call as alleged in this latest correspondence. Those specific statements were:

- '… you don't seem to know a lot about SMART prescribing and I have been asked to have a word with you' (AstraZeneca addressed this point above)
- 'I don't really need to tell you anything!' (AstraZeneca did not believe that this statement in the context referred to by the complainant would in any case constitute a breach of any of the clauses under consideration)
- '..I hope this isn't a problem. I didn't mean to cause any trouble…' (AstraZeneca did not agree that this was necessarily an admission of wrong doing).

Following the appointment with the complainant the representative received a telephone call from the practice manager stating that the complainant was not happy about how and why she had got the appointment with him. From its initial submission, AstraZeneca had further established that the representative asked the practice manager 'where does the doctor want to go with this?' The representative asked the practice manager if the complainant wanted an apology. The practice manager said that she would call the representative back once she had spoken with the complainant. The practice manager telephoned the representative again to say that the complainant would like a written apology and the representative agreed to do that. The representative asked what the complainant was unhappy about and thus what she would be apologizing for and the practice manager said 'that they felt in the middle of things and would get the doctor to write to the representative'. The representative said to the practice manager that she would write an apology to the doctor in response to any letter of complaint from him setting out the specific concerns and that this letter from the doctor could be sent to her home address. This was, as stated by the complainant, before the representative's manager became involved.

Subsequently, the representative discussed the events with her line manager who told her that they were not allowed to write an external apology without Head Office approval. This advice from the manager was not inconsistent with the encouragement AstraZeneca gave its employees to report concerns internally along the management chain or to its compliance function so that appropriate investigation and action could take place. As mentioned in AstraZeneca's initial response, in a telephone conversation with the doctor on 18 March, the manager informed the complainant that any letter of apology from the representative would require Head Office approval, and as a first step in the process of addressing his concerns, the manager asked the doctor to submit a written statement setting out the specific points of concern. The doctor declined to do this and requested that in fact, the representative should write a statement first setting out the issues, since she should already know what they were, and respond to them accordingly in an honest manner.

The line manager then contacted head office to report the matter and for advice. An initial investigation into this matter took place on 22 March with the representative. Additionally the AstraZeneca compliance department contacted the practice manager to try to uncover the complainant's specific concerns and was told that the complainant did not wish to discuss the matter and would like a copy of AstraZeneca's complaints procedure. AstraZeneca then wrote to the complainant on 29 April requesting information on concerns that he had.

In summary, the AstraZeneca representative and manager concerned believed they were acting in good faith in response to a recommendation from a practice nurse when booking the appointment and for the reasons detailed above.

PANEL RULING

The Panel noted its role was to determine whether or not there had been a breach of the Code. As acknowledged by the complainant some of his concerns were not matters within the scope of the Code. The Panel had to restrict its consideration to those matters which fell within the scope of the Code; whether practice policy had been adhered to in relation to the initial conversation with the practice nurse, whether the representative's comments disparaged the complainant and whether Symbicort Smart was promoted without due comparison or justification.

The Panel noted that the parties' accounts differed markedly. It was difficult in such circumstances to determine where the truth lay. The Panel noted that it was for the complainant to establish his case on the balance of probabilities.

The complainant alleged that the representative had explained that a practice nurse had stated that the complainant did not know a lot about Symbicort SMART and suggested that the representative have

a word with the complainant. This was denied by AstraZeneca which stated that on arrival at the GP practice a practice nurse gestured the representative and her line manager to come into her office. They were not made aware of any practice policy regarding such calls. According to the representative and her line manager this nurse suggested they see the complainant to discuss the use of Symbicort SMART in asthma patients including concomitant use of the blue inhaler. The complainant stated that all of his practice nurses denied making such comments. The Panel also noted the complainant's allegation that the representative's attitude during the interview was insensitive and unprofessional and that the promotion was without due comparison or justification. This was denied by AstraZeneca which referred to the contemporaneous note of its representative. The representative in question had not been at work and AstraZeneca had been unable to comment on the complainant's further information. The complainant provided a very full account of the interview. It was clear that the complainant had been upset. Representatives' calls should not cause inconvenience to those upon whom they call.

The Panel decided that it was not possible to determine on the balance of probabilities precisely what had occurred. The Panel noted that extreme dissatisfaction must be present on the part of a complainant before he/she was moved to submit a complaint. Nonetheless, taking all the evidence into account the Panel decided that it was not possible to determine precisely what had occurred and thus ruled no breach of Clauses 2, 7.2, 8.2 and 15.2.

Complaint received **16 May 2010**

Case completed **6 August 2010**

SPECIALIST DIABETES REGISTRAR v NOVO NORDISK

Promotion of Victoza

A specialist registrar in diabetes complained that, having recently undertaken some continuing medical educational (CME) sponsored by Novo Nordisk, he had received a follow-up email about Victoza (liraglutide) from a third party provider in the US. The email thanked the complainant for viewing the CME module 'Role of GLP-1 [Glucagon-like peptide-1] Agonists in Type 2 Diabetes Therapy' supported by an independent educational grant from Novo Nordisk, Inc. A number of key discussion points were listed in the email.

Whilst the complainant welcomed the educational opportunity he was concerned that this had been hijacked to promote liraglutide. For example, the email referred to the LEAD-6 study but there was an ambiguity and lack of clarity about the precise doses of the medicines used in that study which was misleading as was the suggestion that liraglutide was specifically recommended in the US and European guidelines cited. There was also ambiguity in the discussion of the comparative efficacy and safety of liraglutide vs exenatide which was misleading. The complainant was more seriously concerned about the misleading and incorrect safety information about the use of liraglutide in patients with renal disease.

In the CME module, a section entitled 'Differentiating Incretin Therapies: Focus on Liraglutide' stated that 'As exenatide is extensively cleared by the kidneys, it is not recommended in patients with a creatinine clearance below 30ml/minute or in those with [end-stage renal disease]. In contrast, the pharmacokinetics of liraglutide are unchanged in patients with different stages of renal impairment and treatment with liraglutide was not associated with an increased risk of adverse events'.

This was at odds with the liraglutide prescribing information which was not provided. The latter stated: 'Renal impairment: No dose adjustment is required for patients with mild renal impairment (creatinine clearance 60-90ml/min). There is very limited therapeutic experience in patients with moderate renal impairment (creatinine clearance of 30-59ml/min) and no therapeutic experience in patients with severe renal impairment (creatinine clearance below 30ml/min). Victoza can currently not be recommended for use in patients with moderate and severe renal impairment including patients with end stage renal disease (see section 5.2)'.

The complainant stated that this misinformation endangered patients and was unacceptable particularly when disseminated in the guise of education. The complainant was certain that the notable and authoritative signatures to the email in question would not have endorsed the information.

In response to a request for further information, the complainant stated that he had completed a form and provided his email and acknowledged his interest in being contacted by the US provider in relation to this particular module, amongst others; this form was available at a Novo Nordisk stand at a meeting in December 2009. Subsequently, he was invited to complete an online registration following an email from the US provider and he also agreed to receive updates for other diabetes related CME modules. He had also been given, by the company's sales representatives, a similar form, more recently when he attended two meetings jointly organised by Novo Nordisk and a UK third party education provider.

The detailed response from Novo Nordisk is given below.

The Panel noted that the complainant had stated that he had completed a form indicating his interest in the module at issue; he alleged that the form was available on the Novo Nordisk UK stand at a meeting in December 2009. He had subsequently been offered another form at two meetings jointly organised by Novo Nordisk and a UK third party education provider. Novo Nordisk denied that there were any forms or materials on its stands at the two meetings in December 2009 which invited attendees to register for the module in question or any other educational programme provided by the US provider. Novo Nordisk also submitted it was highly unlikely that the UK provider would offer services from the US provider. Novo Nordisk stated that it had not told any UK health professionals about the US programme.

The Panel noted the difference in the parties' accounts regarding the role of Novo Nordisk in the UK and considered that it was difficult to take this case further. The complainant was not prepared to disclose his identity; the identity of the Novo Nordisk representatives alleged to have given him the form was unknown. The Panel noted that the complainant had agreed to receive updates from the US third party provider for other diabetes related modules.

The Panel noted that the programme was sponsored by Novo Nordisk Inc in the US; Novo Nordisk UK submitted that it had not directed any UK health professional to the site. The Panel noted that nonetheless Novo Nordisk UK was responsible under the Code for the acts or omissions of its overseas affiliates that came within the scope of the Code. The email received by the complainant referred to the FDA, ie US, approval of Victoza, as of January 2010. Victoza had, however, been

available in the UK since 30 June 2009. It thus appeared that the email was directed to a US audience. There was no evidence that Novo Nordisk in the US had encouraged UK health professionals to register for the module in question. The activities of Novo Nordisk Inc in the US with non UK health professionals was not covered by the Code. Nevertheless the Panel was concerned about the allegations which related to the appropriate use of Victoza in renal impairment.

Noting that that a complainant had the burden of proving a complaint on the balance of probabilities, the Panel considered that, on the information provided, there had been no breach of the Code.

A specialist registrar in diabetes complained about the promotion of Victoza (liraglutide) by Novo Nordisk Limited.

COMPLAINT

The complainant had recently undertaken some continuing medical education (CME) training sponsored by Novo Nordisk and had received the following email sent by a third party provider in the US:

'Thank you for recently viewing the following activity on [US third party provider]: Role of GLP-1 [Glucagon-like peptide-1] Agonists in Type 2 Diabetes Therapy. Supported by an independent educational grant from Novo Nordisk, Inc.

To reinforce the educational impact of this activity, the key discussion points are listed below:

> Despite considerable advances in diabetes therapy over the last 10 years and the development of new treatment guidelines to help clinicians make the right therapeutic choices for their patients, many people with type 2 diabetes do not reach the glycemic target set by the ADA/EASD [American Diabetes Association/European Association for the Study of Diabetes].
>
> Once-daily liraglutide FDA [Food and Drug Administration] approved as of January 2010) and twice-daily exenatide belong to the newest class of diabetes drugs, known as GLP-1 receptor agonists.
>
> They address many of the unmet needs of diabetes patients, including weight loss, low risk of hypoglycemia, and ease of use. Consequently, they are likely to become prominent therapeutic tools in the treatment of type 2 diabetes. Current ADA/EASD guidelines recommend GLP-1 receptor agonists as second-line therapeutics, after metformin and sulphonylurea treatment have failed to maintain glycemic targets.
>
> The [Liraglutide Effect and Action in Diabetes] LEAD-6 study is the first head-to-head comparison of liraglutide and exenatide. It was designed to directly compare the safety and efficacy of liraglutide and exenatide in a 26-week, randomized, open-label study. LEAD-6 data showed that liraglutide was significantly more effective at reducing glycated haemoglobin (HbA1c) levels than exenatide, and that more patients achieved HbA1c targets with liraglutide. Fasting plasma glucose reduction was also superior with liraglutide; however, exenatide was more effective at controlling postprandial blood glucose. Weight loss was comparable between treatment groups, whereas beta-cell function improvement was more significant in the liraglutide group.
>
> In terms of safety, hypoglycaemia was significantly less frequent with liraglutide, and other adverse events were similar between treatment groups. Nausea was the main adverse event for both treatment groups but was less persistent with liraglutide than with exenatide. The results of the LEAD-6 study suggest that once-daily liraglutide may be more effective and better tolerated than twice-daily exenatide when added to metformin and/or sulphonylureas. However, exenatide may be more suitable for patients experiencing particularly high postprandial glucose levels. These findings were consistent with indirect comparisons of early-phase studies of the two therapies.
>
> GLP-1 receptor agonists are likely to replace sulphonylureas in early treatment in many patients with type 2 diabetes in the future.
>
> These therapies may also have a role in combination with basal insulin once more data emerge. Additional GLP-1 receptor agonists are currently in development, including once-weekly formulations.'

Whilst the complainant welcomed the educational opportunity he was concerned that this had been hijacked to promote liraglutide. For example, the ambiguity and lack of clarity about the precise doses of the medicines used in the LEAD-6 study was very misleading as was the suggestion that this medicine was specifically recommended in the guidelines mentioned; it was not even mentioned in the National Institute for Health and Clinical Excellence (NICE) guidelines whereas exenatide was. The discussion of the comparative efficacy and safety of the two GLP-1 agonists was ambiguous and misleading. The complainant was more seriously concerned about the misleading and incorrect safety information about the use of this medicine in patients with renal disease.

In the CME module, a section entitled 'Differentiating Incretin Therapies: Focus on Liraglutide', stated that 'As exenatide is extensively cleared by the kidneys, it is not recommended in patients with a creatinine clearance below 30ml/minute or in those with ESRD [end-stage renal disease]. In contrast, the pharmacokinetics of liraglutide are unchanged in patients with different stages of renal impairment and treatment with liraglutide was not associated with an increased risk

of adverse events'.

This was at odds with the liraglutide prescribing information which was not provided. The latter stated that 'Renal impairment: No dose adjustment is required for patients with mild renal impairment (creatinine clearance 60-90ml/min). There is very limited therapeutic experience in patients with moderate renal impairment (creatinine clearance of 30-59ml/min) and no therapeutic experience in patients with severe renal impairment (creatinine clearance below 30ml/min). Victoza can currently not be recommended for use in patients with moderate and severe renal impairment including patients with end stage renal disease (see section 5.2)'.

The complainant stated that this misinformation endangered patients and was unacceptable particularly when disseminated in the guise of education. The complainant was certain that the notable and authoritative signatures to the email above would not have endorsed this questionable information.

When writing to Novo Nordisk, the Authority asked it to comment in relation to Clauses 2, 4.1, 7.2, 7.3, 7.4, 7.9, 9.1, 9.9 and 12.1 of the Code.

RESPONSE

Novo Nordisk noted that the complaint concerned a US third party online educational programme 'Role of GLP-1 Agonists in Type 2 Diabetes Therapy'.

Novo Nordisk did not know about the programme until it received the complaint, and as such Novo Nordisk Limited (UK) did not influence its content or development. Given this was not a UK-initiated site, it had not been certified for use within the UK and Novo Nordisk Limited had not told any UK health professionals about the programme.

The programme referred to the involvement of Novo Nordisk Inc, which was part of the Novo Nordisk Group based in the US. Novo Nordisk understood that Novo Nordisk Inc had not directed any UK health professionals to this site. Novo Nordisk had no way of knowing whether the complainant or any other UK health professionals found the programme as a result of a self-initiated internet search or had received an email regarding its availability. Novo Nordisk understood that the US third party provider might communicate with its registered users – a copy of its registration form which all health professionals were required to complete before gaining access to the website was provided. This included explicit consent for materials relevant to the health professional's area of expertise to be emailed to them.

Given that Novo Nordisk had not influenced the sponsorship, content, development or promotion of the programme, and it understood that Novo Nordisk Inc had not promoted this site to UK health professionals, Novo Nordisk denied breaches of Clauses 2, 4.1, 7.2, 7.3, 7.4, 9.1 and 12.1.

Novo Nordisk further noted that the authors of the email in question were not employees of Novo Nordisk Limited, nor of Novo Nordisk Inc.

FURTHER COMMENTS FROM THE COMPLAINANT

The Panel asked the complainant how he knew about the modules and whether he had signed any agreement with the US third party to access its educational modules that included giving permission to receive follow-up emails.

The complainant stated that he had completed a form and provided his email and acknowledged his interest in being contacted in relation to this particular module, amongst others; this form was available at the Novo Nordisk stand at the December 2009 meeting of the UK Primary Care Diabetes Society (PCDS). Subsequently, he was invited to complete an online registration following an email from the US third party during which he also agreed to receive updates for other diabetes related CME modules. He had also been given, by the company's sales representatives, a similar form, more recently when he attended two meetings jointly organised by Novo Nordisk and a UK third party education provider which he did not require as he was already registered with the US provider.

Novo Nordisk was invited to comment on this information.

FURTHER COMMENTS FROM NOVO NORDISK

In relation to the December UK PCDS meeting, Novo Nordisk stated that it sponsored a satellite symposium prior to the 2009 Scottish PCDS Conference 'Type 2 Diabetes' held in Glasgow on 7 December 2009 and secondly the 'Diabetes Inpatient Conference' in London on 14 December 2009. Copies of the registration forms, together with the agendas for these meetings, were provided. Novo Nordisk confirmed that no forms or information on the stands of either of these meetings invited attendees to register for the US educational modules at issue.

Novo Nordisk stated that it worked with the UK third party education provider from time to time. A copy of the flyer which highlighted the 2010 Insulin Management Workshops, sponsored by Novo Nordisk, was provided. This was the only material which Novo Nordisk's sales representatives had been given in relation to these joint meetings.

Novo Nordisk noted that the UK third party education provider it worked with and the US one named by the complainant were direct competitors; it was highly unlikely that the UK provider would have any information concerning US services at its meetings.

At each of the meetings referred to by the complainant, a standard set of materials was on the Novo Nordisk stands. Details were provided.

Novo Nordisk was concerned that the complainant had made unsubstantiated allegations, given that he had not provided the forms at issue and could not clarify as to where he had obtained them. In order for Novo Nordisk to instigate a proper investigation it needed details from the complainant as to which meetings he was referring to, so that it could check its systems in relation to the documented activities of its sales representative in the relevant geographical area etc on the relevant dates.

PANEL RULING

The Panel noted that the complainant had stated that he had completed a form indicating his interest in the US module at issue; he alleged that the form was available on the Novo Nordisk UK stand at a meeting in December 2009. He had subsequently been offered another form at two meetings jointly organised by Novo Nordisk and a UK third party education provider. Novo Nordisk denied that there were any forms or materials on its stands at the two meetings in December 2009 inviting attendees to register for the US module in question or any other educational programme provided by the US provider. Novo Nordisk also submitted it was highly unlikely that the UK third party education provider it worked with would offer the competitor's services. Novo Nordisk stated that it had not told any UK health professionals about the US programme.

The Panel noted the difference in the parties' accounts regarding the role of Novo Nordisk in the UK and considered that it was difficult to take this case further. The complainant was not prepared to disclose his identity to Novo Nordisk and the identity of the Novo Nordisk representatives alleged to have given him the form was unknown. The Panel noted that the complainant had agreed to receive updates from the US provider for other diabetes related modules.

The Panel noted that the programme was sponsored by Novo Nordisk Inc in the US; Novo Nordisk UK submitted that it had not directed any UK health professional to the site. The Panel noted that nonetheless Novo Nordisk UK was responsible under the Code for the acts or omissions of its overseas affiliates that came within the scope of the Code. The US email received by the complainant referred to the FDA, ie US, approval of Victoza, as of January 2010. Victoza had, however, been available in the UK since 30 June 2009. It thus appeared that the email was directed to a US audience. There was no evidence that Novo Nordisk in the US had encouraged UK health professionals to register for the module in question. The activities of Novo Nordisk Inc in the US with non UK health professionals was not covered by the Code. Nevertheless the Panel was concerned about the allegations which related to the appropriate use of Victoza in renal impairment.

Noting that that a complainant had the burden of proving a complaint on the balance of probabilities, the Panel considered that, on the information provided, there had been no breach of the Code. Thus the Panel ruled no breach of Clauses 2, 4.1, 7.2, 7.3, 7.4, 7.9, 9.1, 9.9, and 12.1.

Complaint received **18 May 2010**

Case completed **16 August 2010**

CASE AUTH/2320/5/10

ANONYMOUS v ASTRAZENECA

Promotion of Symbicort

An anonymous, uncontactable complainant alleged that incorrect information had been given by an AstraZeneca representative during the course of promoting Symbicort Turbohaler (budesonide plus formoterol). Symbicort was indicated in the regular treatment of asthma where the use of a combined inhaled corticosteroid and long-acting beta2-agonist was appropriate.

The complainant noted that the representative stated that a pressurised metered dose inhaler (pMDI), with good technique, delivered only 10-15% of the dose to the lungs compared with 30% achieved with the Turbohaler. The impression given was that the Turbohaler always achieved better lung deposition than an MDI. A leavepiece, entitled 'Clinically Effective Inspiratory Flow', stated: 'Turbohaler is effective at a peak inspiratory flow (PIF) of around 30L/min, delivering 15% of dose to the lung (a pressurised MDI, with good inhalation technique, delivers 10 -15%).' and 'Doubling the PIF to 60L/min increases the lung deposition to about 30%'.

The complainant looked into the matter and noted that lung deposition with MDIs containing ciclesonide was over 50% and with beclometasone was either 36% or 52%, depending on whether the MDI was Clenil or Qvar. Consequently, the complainant was very cautious about the information provided by AstraZeneca and its representative.

The detailed response from AstraZeneca is given below.

The Panel noted AstraZeneca's submission that the bracketed part of the claim 'Turbohaler is effective at a peak inspiratory flow (PIF) of around 30L/min, delivering ~15% of nominal dose to the lung (a pressurised MDI, with good inhalation technique, delivers 10-15%)' was true for the majority of pMDIs used in the UK but not for Alvesco, Clenil and Qvar. The claim, however, was not qualified, it appeared that no pMDI delivered more than 10-15% of the nominal dose which was not so; Alvesco delivered over 50%, Clenil 36% and Qvar 52%.

The Panel did not accept AstraZeneca's submission that, taken in its entirety, health professionals would understand the claim to mean that at a PIF of around 30L/min the amount of medicine delivered to the lung by a Symbicort Turbohaler was comparable to that of the more common pMDIs. It appeared that at a PIF of around 30L/min the dose delivered from the Turbohaler was comparable to that delivered by all pMDIs which was not so. The Panel considered that the claim as a whole presented a misleading comparison which could not be substantiated. Breaches of the Code were ruled.

The Panel noted that the claim 'Doubling the PIF to 60L/min increases lung deposition to about 30%' was true for the Turbohaler. However, given the context in which it appeared ie immediately below the comparative claim discussed above, it appeared that at a PIF of 60L/min lung deposition with a Turbohaler would be better than with all pMDIs which was not so. Breaches of the Code were ruled.

The Panel noted its rulings above and considered that high standards had not been maintained. A breach of the Code was ruled which was upheld on appeal by AstraZeneca.

The Panel noted that the complainant alleged that the representative had stated that a pMDI with good technique delivered only 10-15% of the dose to the lungs compared with 30% achieved with the Turbohaler. The Panel considered that it was difficult to know what had been said between the parties; a judgement had to be made on the available evidence. The complainant was anonymous and non-contactable and had not identified the representative. The Panel considered that the statement allegedly made by the representative was misleading. Nonetheless, it was based on the claims in the leavepiece and, in that regard, the representative was only following his/her brief. The Panel considered that the matter was covered by its rulings of breaches of the Code above and thus the Panel ruled no breach of the Code.

An anonymous, uncontactable complainant alleged that information given by a representative of AstraZeneca UK Limited, during the course of promoting Symbicort Turbohaler (budesonide plus formoterol), was incorrect. Symbicort was indicated in the regular treatment of asthma where the use of a combined inhaled corticosteroid and long-acting beta2-agonist was appropriate.

COMPLAINT

The complainant noted that the representative stated that a pressurised metered dose inhaler (pMDI), with good technique, delivered only 10-15% of the dose to the lungs compared with 30% achieved with the Turbohaler. The impression given was that the Turbohaler always achieved better lung deposition than an MDI. The representative provided a leavepiece entitled 'Clinically Effective Inspiratory Flow' (ref CZ001110SYMB) which stated:

'Turbohaler is effective at a peak inspiratory flow (PIF) of around 30L/min, delivering 15% of dose to the lung (a pressurised MDI, with good inhalation technique, delivers 10 -15%).'

and

'Doubling the PIF to 60L/min increases the lung deposition to about 30%.'

The complainant looked into the matter and noted that lung deposition with MDIs containing ciclesonide was over 50% and with beclometasone was either 36% or 52%, depending on whether the MDI was Clenil or Qvar.

Consequently, the complainant was very cautious about the information provided by AstraZeneca and its representative.

When writing to AstraZeneca, the Authority asked it to respond in relation to the requirements of Clauses 7.2, 7.3, 7.4, 9.1 and 15.2 of the Code.

RESPONSE

AstraZeneca stated that the leavepiece was developed to inform health professionals about the range of clinically effective peak inspiratory flow (PIF) rates for the Symbicort Turbohaler device in asthmatic patients.

'Turbohaler is effective at a peak inspiratory flow (PIF) of around 30L/min, delivering ~15% of nominal dose to the lung (a pressurised MDI, with good inhalation technique, delivers 10-15%)'

The first part of this claim stated that the Symbicort Turbohaler was effective at a PIF of around 30L/min and delivered approximately 15% of nominal dose to the lung. Efficacy at flow rates around 30L/min had been demonstrated in clinical studies (Engel *et al* 1992, Pedersen *et al* 1990).

The part of the claim in brackets 'a pressurised MDI, with good inhalation technique, delivers 10-15%' referred to the fact that 10 -15% of the metered dose of the pharmacological agent from the more commonly used types of pMDI was delivered to the lung.

AstraZeneca noted that the pMDI market was segmented into two parts: those pMDIs which delivered approximately 10 -15% of pharmacological agent to the lungs and those which delivered a higher percentage of pharmacological agent to the lungs including Alvesco (ciclesonide) at over 50%, Clenil (beclometasone) at 36%, and Qvar (beclometasone) at 52%, all listed by the complainant. This was important because the pMDIs which delivered a higher percentage of pharmacological agent to the lungs represented only a small proportion of overall pMDI usage. Data from IMS in March 2009 which measured UK sales of these less common, by market share, pMDIs showed that they only made up approximately 10% of the total pMDI market with the more common pMDIs making up approximately 90% of sales. IMS data from April 2010 demonstrated that these less common pMDIs still only accounted for approximately 15% of the market, with the remainder made up of the more common pMDIs.

Indeed, in the scientific literature it was well established that the more common pMDIs delivered in the range of approximately 10-15% of the nominal dose, with similar figures quoted in recent peer-reviewed publications. Lavorini and Fontana (2009) stated that '… no more than ~20% of the emitted dose reaches the lungs'. Vincken *et al* (2010) stated that 'Attaching a spacer to a pMDI also filters out the non-respirable particles and slows down the emitted aerosol, such that pulmonary deposition increases from around 10% using a pMDI to 20% or more using a pMDI plus spacer'.

The fact that in clinical practice the more common pMDIs required separate consideration was reflected in the most recent British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) guidelines. Section 5.4, which referred to relative effects of different inhaled steroid pMDI products, stated, 'It is important to differentiate Qvar from other HFA beclometasone products. Many studies now show Qvar equivalence at half the dose of CFC BDP, whereas non-Qvar HFA BDP pMDI products show equivalence at 1:1 dosing'.

Therefore, it was clear that a health professional reviewing this item would assume that the claim at issue compared Symbicort Turbohaler with these more common pMDIs which made up the vast majority of the pMDIs and not with the less common pMDIs such as Qvar and Clenil as alleged by the complainant.

Therefore, this claim in its entirety would be understood by the health professional to indicate that at a PIF of around 30L/min the amount of drug delivered to the lung by the Symbicort Turbohaler was comparable to that of the more common pMDIs as outlined above.

Relevant to this, Borgstrom *et al* (1994), which was cited in the leavepiece, stated that 'Drug deposition in the lungs at 36L/min is at least as good with Turbohaler as with a correctly used pressurised MDI …'. This was further substantiated in a clinical review which was also referenced in the leavepiece and which examined delivery devices for inhaled asthma drugs. The authors stated 'At lower flow rates the deposition from Turbohaler resembles that seen when a patient with good coordination uses a classic pMDI' (Selroos *et al* 1996).

Therefore, although the complainant questioned the accuracy of the claim, and referred to examples of the less common pMDIs which delivered higher percentages of medicine deposition in the lungs, over 50% for Alvesco (ciclesonide), 36% for Clenil

(beclometasone) and 52% for Qvar (beclometasone), without further qualification the health professional would interpret the claim to refer to the more common pMDIs.

Based on the above information, AstraZeneca submitted that the claim was a fair and balanced reflection of the overall evidence relating to lung deposition with the Symbicort Turbohaler and the more common pMDIs and was capable of substantiation. Therefore, AstraZeneca did not consider that Clauses 7.2, 7.3 or 7.4 had been breached.

Furthermore, AstraZeneca did not believe that the use of the claim in the leavepiece did not maintain high standards and was in breach of Clause 9.1.

'Doubling the PIF to 60L/min increases the lung deposition to about 30%'

This claim referred to the fact that increasing the PIF to 60L/min increased the lung deposition of Symbicort Turbohaler to about 30%. Thorsson *et al* (1994) determined the pulmonary and systemic availability of budesonide after inhalation from the Symbicort Turbohaler, and also from a pMDI in healthy volunteers. The subjects were trained to breathe out to residual volume, and then to inhale at a flow of 60L/min for Turbohaler, and 30L/min for pMDI. The bioavailability was calculated using two methods. The pulmonary availability, calculated using the first method, was 32% and 15% for Symbicort Turbohaler and pMDI, respectively, and using the second method, 32% and 18%, respectively.

Furthermore, Selroos *et al* stated that most pMDIs gave deposition figures of around 10 -15% of the metered dose (at a flow rate of around 30L/min), whilst the use of the Turbohaler resulted in deposition of 20 - 35% of the metered dose at a flow of ≥40L/min.

Therefore, with reference to the Symbicort Turbohaler this claim was fair, balanced, not misleading and capable of substantiation. AstraZeneca did not believe that there had been a breach of Clauses 7.2, 7.3, or 7.4. Furthermore, AstraZeneca did not believe that the use of the claim in the leavepiece did not maintain high standards, relating to Clause 9.1.

AstraZeneca noted that the representative had allegedly stated that a pMDI, with good technique, delivered only 10 -15% of the dose to the lungs, compared with the 30% achieved with the Turbohaler.

AstraZeneca further noted that the complainant had not identified the representative. Without further information, it was not possible to investigate this aspect of the complaint, including any specific training the representative might have received. However, AstraZeneca provided a copy of a relevant training presentation ('Devices' Powerpoint presentation, ref CZ003316, date of preparation, February 2010) that was used as part of the induction programme for all representatives in relation to the use of inhalers, although the company did not have briefing materials for the specific leavepiece. This training on relevant aspects of inhaler devices gave the representatives the necessary knowledge to be able to deliver the content of materials, such as the leavepiece, in a compliant and factual fashion. For example, slides 12-31 of the presentation provided information about inhaler delivery systems including pMDIs and dry powder devices (DPIs). Of particular relevance to the current complaint, slide 29 informed the representative about inspiratory flow rate and lung deposition with the Symbicort Turbohaler: '30L/min is the inspiratory flow rate needed to achieve a clinical response with the TBH = 15% deposition, as IFR increases, the amount of drug deposited increases, up to a maximum of around 30%, at the IFR of 60L/min'. Also of specific relevance to the contested claims, slide 30 referred to lung deposition levels with different devices including Seretide Evohaler (pMDI), Seretide Accuhaler (DPI) and Symbicort Turbohaler (DPI).

AstraZeneca considered that on the balance of probabilities, taking into account the content of the leavepiece and relevant associated training materials, it was likely that the representative would have stated the claim as set out in the leavepiece that was the subject of this complaint: 'Turbohaler is effective at a peak inspiratory flow (PIF) of around 30L/min, delivering ~15% of nominal dose to the lung (a pressurised MDI, with good inhalation technique, delivers 10-15%)'.

Therefore, taking all the above evidence into account, and on the balance of probabilities in terms of what the representative was likely to have said to the complainant, and the content of the leavepiece, AstraZeneca did not understand how the complainant was left with the impression that the Turbohaler always achieved better lung deposition than an MDI. This was never AstraZeneca's intention and such a claim had never formed any part of the promotional activity for Symbicort Turbohaler in the UK.

AstraZeneca did not believe that the representative had not maintained high standards and therefore did not believe that there had been a breach of Clause 15.2. The company also strongly considered that there had been no breach of Clause 9.1 relating to high standards.

In summary, AstraZeneca did not believe that there had been breaches of Clauses 7.2, 7.3, 7.4, 15.2 and 9.1.

PANEL RULING

The Panel noted AstraZeneca's submission that the bracketed part of the claim 'Turbohaler is effective at a peak inspiratory flow (PIF) of around 30L/min, delivering ~15% of nominal dose to the lung (a pressurised MDI, with good inhalation technique,

delivers 10-15%)' was true for the majority of pMDIs used in the UK but not for Alvesco, Clenil and Qvar. The claim, however, was not qualified, it appeared that no pMDI delivered more than 10-15% of the nominal dose which was not so; Alvesco delivered over 50%, Clenil 36% and Qvar 52%.

The Panel did not accept AstraZeneca's submission that, taken in its entirety, health professionals would understand the claim to mean that at a PIF of around 30L/min the amount of medicine delivered to the lung by a Symbicort Turbohaler was comparable to that of the more common pMDIs. It appeared that at a PIF of around 30L/min the dose delivered from the Turbohaler was comparable to that delivered by all pMDIs which was not so. The Panel considered that the claim as a whole presented a misleading comparison which could not be substantiated. Breaches of Clauses 7.2, 7.3 and 7.4 were ruled.

The Panel noted that the claim 'Doubling the PIF to 60L/min increases lung deposition to about 30%' was true for the Turbohaler. However, given the context in which it appeared ie immediately below the comparative claim discussed above, it appeared that at a PIF of 60L/min lung deposition with a Turbohaler would be better than with all pMDIs which was not so. Breaches of Clauses 7.2, 7.3 and 7.4 were ruled.

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

The Panel noted that the complainant alleged that the representative had stated that a pMDI with good technique delivered only 10-15% of the dose to the lungs compared with 30% achieved with the Turbohaler. The Panel considered that it was difficult to know what had been said between the parties; a judgement had to be made on the available evidence. The complainant was anonymous and non contactable and had not identified the representative. The Panel considered that the statement allegedly made by the representative was misleading. Nonetheless, it was based on the claims in the leavepiece and, in that regard, the representative was only following his/her brief. The Panel considered that the matter was covered by its rulings of breaches of the Code above and thus the Panel ruled no breach of Clause 15.2.

APPEAL BY ASTRAZENECA

AstraZeneca noted that although it had accepted the rulings of breaches of Clauses 7.2, 7.3, and 7.4 it did not believe that the reasons set out by the Panel for those rulings were grounds for concluding that high standards were not maintained.

AstraZeneca submitted that, as stated previously, as the complainant had not named the representative in question and as the complainant was anonymous and non-contactable it was not possible to investigate this aspect of the complaint further.

Therefore, AstraZeneca agreed with the Panel's ruling that the matter of what was allegedly stated by the representative was covered by its rulings of the breaches of the Code in relation to the claims in the leavepiece. AstraZeneca therefore restricted its comments below to considerations around the claims in the leavepiece and not to any alleged representative activities.

AstraZeneca noted that Clause 9.1 stated that 'high standards must be maintained at all times' which it believed to be applicable in relation to the content of the challenged leavepiece. The supplementary information to Clauses 9.1 and 9.2 of the Code stated:

'The special nature of medicines and the professional audience to which the material is directed require that the standards set for the promotion of medicines are higher than those which might be acceptable for general commodity advertising.

It follows therefore that certain types, styles and methods of promotion, even where they might be acceptable for the promotion of products other than medicines, are unacceptable.

These include:

- the display of naked or partially naked people for the purpose of attracting attention to the material or the use of sexual imagery for that purpose
- 'teaser' advertising whereby promotional material is intended to 'tease' the recipient by eliciting an interest in something which will be following or will be available at a later date without providing any actual information about it
- the provision of rubber stamps to doctors for use as aids to prescription writing
- the provision of private prescription forms preprinted with the name of a medicine.'

AstraZeneca submitted that although the supplementary information applied specifically to suitability and taste it provided examples of the types of situations where a breach of Clause 9.1 would be applicable. In view of this, although AstraZeneca accepted the Panel's rulings of breaches of Clauses 7.2, 7.3, and 7.4 in relation to the use of the claims in the leavepiece it did not understand in what way the considered use of the claims in the leavepiece compromised the required high standards set out in the Code. AstraZeneca submitted that it had carefully considered the evidence that underpinned the claims at issue and thus a breach of Clause 9.1 was not applicable in this particular case.

AstraZeneca submitted that the leavepiece at issue was developed to inform health professionals of the range of clinically effective PIF rates for the Symbicort Turbohaler device in asthmatic patients.

The complaint referred to two adjacent claims in the leavepiece.

AstraZeneca noted that the first claim at issue was 'Turbohaler is effective at a peak inspiratory flow (PIF) of around 30L/min, delivering ~15% of nominal dose to the lung (a pressurised MDI, with good inhalation technique, delivers 10-15%)' The first part of this claim stated that the Symbicort Turbohaler was effective at PIF of around 30L/min and delivered approximately 15% of nominal dose to the lung. Efficacy at flow rates around 30L/min has been demonstrated in clinical studies (Engel *et al*, Pedersen *et al*). The bracketed part of the claim 'a pressurised MDI, with good inhalation technique, delivers 10-15%' referred to the fact that 10-15% of the metered dose of the pharmacological agent from the more commonly used type, or conventional, pressurised metered dose inhaler (pMDI) was delivered to the lung.

AstraZeneca noted that the pMDI market could be segmented into two parts: the more common pMDIs which delivered approximately 10-15% of pharmacological agent to the lungs, made up the large proportion of the marketplace (also known as conventional pMDIs which were the 'fine' particle inhalers (range ~3-5 microns)), and those which delivered a higher percentage of pharmacological agent to the lungs including Alvesco at over 50%, Clenil at 36%, and Qvar at 52%, all listed by the complainant, which made up a small proportion of the marketplace. Alvesco, Clenil and Qvar were all extra-fine particle inhalers (range ~1-3 microns) which helped to explain their higher levels of lung deposition compared with the conventional pMDIs.

AstraZeneca submitted that the extra-fine particle pMDIs which delivered a higher percentage of pharmacological agent to the lungs represented only a small proportion of overall pMDI usage. IMS data in March 2009 showed that they only made up approximately 10% of the total pMDI market, with the conventional pMDIs making up approximately 90% of sales. IMS data from April 2010 demonstrated that these less common extra-fine particle pMDIs still accounted for approximately only 15% of the pMDI market, with the more common conventional pMDIs accounting for approximately 85% of the pMDI market (April 2010 data provided).

AstraZeneca submitted that in the scientific literature it was well established that the conventional pMDIs delivered approximately 10-15% of the metered dose. Thorsson *et al* reported, in a study comparing the Turbohaler with a pMDI, that 'the pulmonary availability, calculated relative to metered-doses and assuming an oral availability of 13%, was 32% (geometric mean, range 16-59%) for Turbohaler and 15% (range 3-47%) for pMDI'. Additionally, Barry and O'Callaghan (1996) examined the use of spacer devices with MDIs, and stated that 'Proper use requires coordination of inhalation and MDI actuation but, even with optimum technique, less than 15% of the actuated dose reaches the lungs.' This was further substantiated in a clinical review (Selroos *et al*) referenced in the leavepiece, which examined delivery devices for inhaled asthma medicines. Here, it stated: 'At lower flow rates the deposition from Turbohaler resembles that seen when a patient with good coordination uses a classic pMDI'. Further to this, Lavorini and Fontana stated that '…no more than ~20% of the emitted dose reaches the lungs.' Vincken *et al* stated that 'Attaching a spacer to a pMDI also filters out the non-respirable particles and slows down the emitted aerosol, such that pulmonary deposition increases from around 10% using a pMDI to 20% or more using a pMDI plus spacer.'

AstraZeneca further noted that Newman and Chan (2008) reviewed data around fine particle fractions and lung deposition across 33 different inhalers including pMDIs and showed that the vast majority of pMDIs (CFC and HFA) tested were clustered around the 10-15% lung deposition range. The only pMDI in this analysis with a significantly higher lung deposition value contained an add-on device and therefore was not relevant to this discussion.

AstraZeneca submitted that the fact that in clinical practice these less common, extra fine particle pMDIs required separate consideration was reflected in the most recent BTS/SIGN guidelines (2009) Section 5.4, which referred to relative effects of different inhaled steroid pMDI products, stated, 'It is important to differentiate Qvar from other HFA beclometasone products. Many studies now show Qvar equivalence at half the dose of CFC BDP, whereas non-Qvar HFA BDP pMDI products show equivalence at 1:1 dosing'.

Therefore, AstraZeneca submitted that as stated above, the conventional pMDIs were so widely used and prescribed that it considered that health professionals would assume that the contested claim compared Symbicort Turbohaler with these pMDIs (which generally had a lung deposition of around 10-15%), and not with all pMDIs which would include the extra-fine particle pMDIs such as Qvar, Alvesco and Clenil as mentioned by the complainant.

Finally, AstraZeneca also noted the use of the indefinite article 'a' in the bracketed section of the claim. In its ruling the Panel assumed that this claim referred to all pMDIs which was not so. AstraZeneca did not intend to imply that all pMDIs had a lung deposition level of 10-15%. In contrast, the use of the indefinite article ensured exactly the opposite effect, to make clear that this was not intended to be a general statement applicable to all pMDIs. The use of the indefinite article was consistent with AstraZeneca's intention to refer to the more common conventional pMDIs as stated above.

On this basis AstraZeneca intended this claim, in its entirety, to be understood by the health professional to indicate that at a PIF of around 30L/min the amount of medicine delivered to the

lung by the Symbicort Turbohaler was comparable to that of the far more common conventional pMDIs as outlined above. In support of this, Borgstrom *et al* which was referenced in the leavepiece, stated that 'Drug deposition in the lungs at 36 L/min is at least as good with Turbohaler as with a correctly used pressurised MDI ...'.

AstraZeneca accepted the Panel's rulings of breaches of Clauses 7.2, 7.3 and 7.4 but did not agree that this claim was a breach of Clause 9.1 relating to high standards based on the above considerations.

AstraZeneca noted the second claim stated 'Doubling the PIF to 60L/min increases the lung deposition to about 30%'. The Panel had stated that given the context in which this claim appeared ie immediately below the comparative claim discussed above, 'it appeared that at a PIF of 60L/min lung deposition with a Turbohaler would be better than with all pMDIs which was not so'. However, this claim was presented as a separate bullet and was a standalone claim. The intention was that this claim referred to the fact that increasing the PIF to 60L/min increased the lung deposition of Symbicort Turbohaler to about 30%. It was not intended to imply that Symbicort Turbohaler at 60L/min would be better than all pMDIs.

Therefore, although AstraZeneca accepted the Panel's view that the claim could be interpreted in a different way and it had therefore ruled breaches of Clauses 7.2, 7.3 and 7.4 of the Code, AstraZeneca did not believe that it followed that this was an indication that the use of this claim, or indeed the use of both claims in the same leavepiece, constituted a breach of Clause 9.1 relating to high standards based on the above.

To conclude, given the intent of the provision of Clause 9.1, AstraZeneca submitted that a breach of Clause 9.1 was not applicable in this case. AstraZeneca accepted that irrespective of the above considerations relating to the use of the claims at issue in the leavepiece, the Panel had ruled breaches of Clauses 7.2, 7.3, and 7.4. However, AstraZeneca did not believe that breaches of Clause 7 automatically constituted a breach of Clause 9.1.

APPEAL BOARD RULING

The Appeal Board noted from the AstraZeneca representatives at the appeal that the Turbohaler had been on the UK market for over 20 years. In that regard the Appeal Board considered that health professionals should be reasonably familiar with the delivery characteristics of the device. Nonetheless, the leavepiece at issue had been developed to be used reactively with any health professionals concerned that the Symbicort Turbohaler might not be clinically effective at low respiratory flow rates. The leavepiece had been approved for use with doctors, pharmacists and nurses.

The Appeal Board noted that AstraZeneca had not made it clear in the leavepiece that the reference to 'a pressurised MDI' only included the more common 'fine' particle inhalers and not also the less common 'extra-fine' particle inhalers. The Appeal Board rejected AstraZeneca's submission that use of the indefinite article 'a' helped in this regard. In the Appeal Board's view 'a pressurised MDI' implied any pressurised MDI chosen at random.

The Appeal Board noted that the leavepiece sought to inform health professionals about the delivery characteristics of the Turbohaler (which had been available in the UK for a number of years) whilst assuming that they were so familiar with the 'extra-fine' particle inhalers (introduced to the UK market after the Turbohaler) that the claims at issue did not need to be qualified. In the Appeal Board's view, although the majority of health professionals would be experienced in the treatment of asthma and would, at least in general, know about the BTS guidelines with regard to Qvar etc, experience and knowledge in that regard could not be assumed and did not mean that unqualified claims were acceptable; it was beholden upon AstraZeneca to ensure that its claims were clear and could not mislead. In that regard the Appeal Board noted that AstraZeneca had accepted the Panel's rulings of breaches of Clauses 7.2, 7.3 and 7.4. The Appeal Board further noted that if prescribers had been misled by the leavepiece, patient safety might have been adversely affected.

The Appeal Board considered that high standards had not been maintained and it upheld the Panel's ruling of a breach of Clause 9.1. The appeal was thus unsuccessful.

Complaint received **21 May 2010**

Case completed **6 August 2010**

MEDIA/DIRECTOR v ROCHE

Promotion of Tamiflu

An article published in The Financial Times 22 May 2010, entitled 'Roche accused of pressuring employee into illegal Tamiflu deals', reported matters raised during an employment tribunal, alleging that Roche pressurised its sales staff illegally to sell the prescription only medicine (POM) Tamiflu to people who were not doctors and incentivised customers with cash payments.

It was alleged that Roche had promoted Tamiflu to business continuity managers in companies keen to secure supplies of the scarce medicine for private stockpiles amidst growing concerns about a flu pandemic. The article referred to a special business unit, created in 2006 to sell Tamiflu to companies, being set unrealistically high commercial targets given the tight controls on the marketing of POMs. It was stated that there had been no efforts to ensure sales staff only spoke to health professionals and that Roche also sold Tamiflu to intermediary organisations employing medical staff, which in turn would sell the medicine to clients. It was reported that Roche had decided that it could speak about business continuity to non-medical customers provided that it did not mention the efficacy, dose or even the name of the medicine itself.

The article also reported that, to maintain market share, Roche had overcharged the NHS for its medicines by offering discounts from the official price to pharmacists and distributors. It was alleged that the company provided cash payments and discounts on future orders to customers so that they would buy its products rather than lower priced generics or parallel imports.

In accordance with the Authority's Constitution and Procedure the matter was taken up as a complaint by the Director.

The detailed response from Roche is given below.

The Panel noted the allegation that the company pressurised its staff to sell Tamiflu to people who were not doctors. The Code covered the promotion of medicines to members of the health professions and appropriate administrative staff. Thus POMs could be promoted to persons who were not doctors, such as senior NHS managers and the like, so long as the material or activity was relevant and tailored to the audience and otherwise complied with the Code. POMs could not be promoted to the general public.

The Panel noted Roche's submission that the members of the relevant business team would speak to a health professional or the person responsible for continuity planning. Tamiflu would not be promoted to non-health professionals. Staff were given guidelines which stated 'If speaking to a doctor/nurse/medically qualified individual we discuss antivirals/Tamiflu. If speaking to non-medic, we talk generically about supporting their pandemic plan and that we would need to speak to their medical advisor to discuss medical support and POM's' [sic]. Tamiflu support materials could be given to those companies which did not have antivirals in their pandemic plan. The materials were to be supplied to 'medics only' and thereafter the conversation was terminated. For companies with antivirals in their pandemic plan, staff could discuss, *inter alia*, appropriate prescribing models and options and conclude with an order. It was difficult to see how a conversation with a 'non-medic' would fit with these guidelines. The Panel queried whether sufficient instruction in relation to companies without a medically qualified member of staff had been given.

The Panel was concerned that a sales aid which Roche stated in practice was only supplied to health professionals was certified for use with the business community and occupational health. The Panel also queried whether guidelines provided to staff were sufficiently clear about what materials were to be given to who. One document referred to sending a 'Letter/Brochure' to relevant persons 'Pharma – Medic, Others – Business Continuity Manager/General Manager.' This was followed by a list of approved materials but did not specify which were suitable for non-medically qualified people. The business continuity wallet, for example, might contain a sales aid if sent to a doctor. The Panel considered that the instructions to staff regarding the use of materials and about discussions with non-medically qualified persons were not sufficiently clear. Nonetheless taking all the circumstances into account there was no evidence to show that on the balance of probabilities Roche had actually promoted Tamiflu to a non-health professional as alleged. No breach of the Code was ruled.

The article referred *inter alia* to the provision of discounts and cash payments on future orders to customers. Roche noted that reference to discounts or cash equivalent rebates had been made in the tribunal proceedings but there was no reference to cash payments. Roche confirmed that it provided customers with rebates in the form of credit notes. The Panel noted that the supplementary information stated that measures or trade practices relating to prices, margins and discounts which were in regular use by a significant proportion of the pharmaceutical industry on 1 January 1993 were outside the scope of the Code. Prices, margins and discounts were primarily financial terms. In

principle credit notes and discounts which met the requirements of the relevant supplementary information were excluded from the Code. The Panel had no information about the nature of the credit notes provided by Roche. However there was no evidence before the Panel to indicate that inappropriate discounts or cash payments had been made contrary to the provisions of the Code thus no breach was ruled.

An article published in The Financial Times 22 May 2010 was entitled 'Roche accused of pressuring employee into illegal Tamiflu deals'. The author reported matters raised during an employment tribunal case namely that Roche put pressure on its sales staff illegally to sell the prescription only medicine (POM) Tamiflu to people who were not doctors and incentivised customers by providing cash payments.

In accordance with Paragraph 6.1 of the Authority's Constitution and Procedure the matter was taken up with Roche as a complaint by the Director. The author of the article was asked whether he wished to be involved in the case or whether he had any additional information to submit. The author did not respond.

The matters at issue occurred during 2006 and thus the case was considered in relation to the requirements of the 2006 Code under the Constitution and Procedure of the 2008 edition of the Code.

COMPLAINT

The article was about the pressurised selling of Tamiflu to people who were not doctors. It was alleged that Roche had promoted the medicine to business continuity managers in companies keen to secure supplies of the scarce medicine for private stockpiles when there were growing concerns about a flu pandemic.

The article specifically referred to a special business unit, created in 2006 to sell Tamiflu to companies, being set unrealistically high commercial targets given the tight controls on the marketing of POMs. It was stated that there had been no efforts to ensure sales staff only spoke to health professionals and that Roche also sold Tamiflu to intermediary organisations employing medical staff, which in turn would sell the medicine to clients. Additional concerns were whether the discussions with companies over volumes of Tamiflu stock breached competition rules designed to ensure fair allocation of the scarce medicine and whether non-medical customers had the facilities to safely store and track their medicine. It was reported that the Medicines and Healthcare products Regulatory Agency (MHRA) had investigated a complaint from a business continuity manager who received a call from the Roche sales team but subsequently took no action.

It was reported that Roche had decided that it could speak about business continuity to non-medical customers provided that it did not mention the efficacy, dose or even the name of the medicine itself.

Further it was alleged that Roche had overcharged the NHS for its medicines by offering discounts from the official price to pharmacists and distributors to maintain market share. It was alleged that the company provided cash payments and discounts on future orders to customers so that they would buy its products rather than lower priced generics or parallel imports.

When writing to Roche, the Authority asked it to respond in relation to the requirements of Clauses 2, 9.1 and 18.1 of the 2006 Code.

RESPONSE

Roche stated that the allegations were made in the context of an employment tribunal claim by an ex-employee who was aggrieved at being made redundant (the ex-employee claimed the real reason for his dismissal was because he made protected disclosures rather than a genuine redundancy). Although the tribunal hearing had concluded the decision had not been issued.

Roche stated that, with regard to the allegation about cash payments, the article in The Financial Times stated that Roche 'provided cash payments to customers' suggesting that cash was paid to individuals. The journalist had incorrectly reported the evidence. In his evidence to the tribunal, the ex-employee referred to Roche giving discounts or 'cash equivalent' rebates to customers. Roche confirmed that it had provided, and continued to provide, customers with rebates in the form of a credit note. This was standard commercial practice outside the scope of the Code. The ex-employee had not alleged that Roche had paid its customers cash. Indeed the ex-employee told the tribunal that he had never made any protected disclosure regarding inducements to prescribe.

In October 2006 the MHRA informed Roche that it had received a complaint to the effect that the commercial section of The Financial Times had received a telephone call from Roche suggesting that the company should consider purchasing antivirals for treatment and prophylaxis of its own staff (a copy of the letter was provided). There was no allegation that Roche had actually promoted Tamiflu or antivirals generally to the commercial team of The Financial Times. Roche had responded that, *inter alia*, it would only discuss Tamiflu with those people in an individual company involved in continuity planning and/or health professionals within an occupational health department should one exist (a copy of the response was provided). Roche had sought clarity on this statement from the author of the letter and his clear recollection was that this was not meant to imply that Tamiflu was promoted to non-health professionals. In its follow up (a copy of which was provided) the MHRA reminded Roche to ensure that discussions about a POM were limited to appropriate health

professionals. The author of Roche's response to the MHRA stated that although Tamiflu was not promoted to non-health professionals, he recalled reminding staff that they could only discuss Tamiflu with health professionals. Roche had not received any other complaints alleging inappropriate promotion of Tamiflu to private companies.

The ex-employee alleged that in 2006 Roche targeted business continuity managers in the promotion of Tamiflu. Neither The Financial Times article, nor the ex-employee, in his tribunal case, had produced any evidence to show that Roche had inappropriately promoted Tamiflu, and as stated above, the MHRA, at the time, did not rule that Roche had done anything wrong. The ex-employee's evidence to the tribunal was contradictory. On the one hand he alleged that Tamiflu was promoted to business continuity managers, and on the other he stated that he told his team that they could only discuss Tamiflu with a company's doctor. Despite being repeatedly challenged by the judge, the ex-employee was unable to provide any information to back up his claim that he had raised concerns with his managers about the promotion of Tamiflu to people who were not health professionals. Roche's investigation into this matter (including speaking to relevant employees) had failed to uncover evidence that Tamiflu was improperly promoted.

Roche explained that the ex-employee joined the company in 1995. In 2006 he was appointed to a new role reporting to the head of commercial. Roche had been unable to locate a job description but the primary responsibilities were to: manage the head office commercial development team; ensure professional delivery of commercial services within Roche inclusive of product and general commercial strategies through participation in the commercial development group management team; ensure the development of business for Tamiflu in the corporate sector.

This was not a business unit but rather a small team within the commercial department the main aim of which was to develop Tamiflu business within the private sector. Prior to this Roche had not sought to supply Tamiflu to the private sector. However, with the bird flu scare Roche started to receive a lot of requests for advice from companies about continuity planning in the event of a pandemic, including obtaining supplies of Tamiflu to protect their staff. Initially enquiries were handled by the customer services department with questions about Tamiflu being referred to medical information, but due to the increasing number of calls, and recognising the commercial opportunity, the specialist team under the ex-employee's leadership was established. Roche noted that at the time the government had encouraged companies to put in place plans to deal with a flu pandemic, and that antiviral therapy was seen as an important part of any such plan.

The ex-employee and his team would respond to requests from companies seeking supplies of Tamiflu or advice around pandemic planning, or they would proactively contact companies. In the latter case they sought to speak to either the company's occupational health department or the person responsible for business continuity planning. The business aim was to get companies to develop pandemic plans and to consider antivirals as part of their plan. Guidance as to what the Roche team could say to customers was dealt with below.

Process flows relating to call structure and corporate prospecting were provided. These documents which were used by the specialist team as their primary reference tool contained the following guidance for staff: 'If speaking to a doctor/nurse/medically qualified individual we discuss antivirals/Tamiflu. If speaking to non-medic, we talk generically about supporting their pandemic plan and that we would need to speak to their medical advisor to discuss medical support and POMs'.

Roche submitted that the ex-employee's team would speak to either a health professional or the person responsible for continuity planning (which could be the same person). They would use the process flows mentioned above. The business continuity wallet and 'Survive' guidelines would be given to both health professionals and those who were not health professionals. Health professionals might also receive the drug information pack.

The main topic of discussion with non-medical staff was around business continuity plans. Roche staff asked if a company's plans for handling a flu pandemic included the supply of antivirals for employees. There was no evidence that Roche staff promoted Tamiflu in particular or antivirals in general to non-medical staff. If customers wanted to discuss Tamiflu they were told to do so through their occupational health department/medical adviser.

As a POM Tamiflu would only be supplied to organisations with one of the following: a wholesale dealer's licence; a registered pharmacy; a qualified doctor who would store the medicine under his/her own medical supervision (in this case Roche would check the doctor's General Medical Council number).

The journalist had incorrectly reported the evidence that was given to the employment tribunal. The ex-employee made no allegations about cash being paid to customers, and he specifically stated in evidence that he had not made any public interest disclosure relating to inducements to prescribe. He did, however, mention that Roche gave 'cash equivalent' rebates. Roche confirmed that it had provided, and continued to provide, rebates in the form of a credit note. This was standard commercial practice outside the scope of the Code.

Roche stated that the allegations reported in The Financial Times article were vague and not supported by any evidence. There were just the

bald assertions that Tamiflu was promoted to business continuity managers and that the company provided cash payments to customers. The ex-employee, in his evidence to the employment tribunal, made no allegations about cash payments, and he was unable to provide any specific details relating to improper promotion of Tamiflu. Roche had found no evidence that Tamiflu was promoted to non-medical staff. The MHRA in 2006 did not express any concerns about Roche's activities. Roche submitted that there was no breach of Clauses 2, 9.1 or 18.1 of the Code.

Roche subsequently provided a copy of the reserved judgement of the employment tribunal. Roche noted that the judgement did not mention cash payments to customers. Roche noted the parts of the judgement relevant to Tamiflu and a statement that 'on our findings of fact we are not satisfied that there was a disclosure of information which tended to show any failure in relation to the matters the claimant raised'.

In response to a request for further information from the Panel, Roche explained that the business continuity wallet would be provided to both health professionals and non-health professionals. This would be sent as a follow up to telephone contact that Roche made with a company, or would be left with a company representative responsible for continuity of planning following a meeting (that might be either a health professional or a non-health professional). The 'BC [business continuity] Wallet' and the 'Brochure' mentioned in the purple box at the bottom left of the Process for Corporate Prospecting were the same thing. If sent by post the wallet would be accompanied by a letter.

The wallet would have contained the 'Survive' guidelines. Health professionals would also have received as part of the pack a sales aid (referred to as 'marketing leavepiece' in the 'Process for 1:1 Call Structure').

The sales aid was certified as material for use with 'the Business Community and Occupational Health'. As the sales aid was a promotional item it should only have been certified for use with health professionals. However, according to one of the ex-employee's team who was still with Roche the certificate did not accurately reflect the intended audience, which was health professionals. The same individual had also confirmed that his recollection was that the sales aid was in practice only ever provided to health professionals. Thus whilst the audience stated in the certificate was not accurate (and this perhaps reflected the fact that it was created when Roche's Code knowledge and processes were not what they should have been), the sales aid was not in practice used inappropriately.

The e-mail address and freephone number referred to in both the wallet and the 'Survive' guidelines enabled continuity managers and health professionals to contact members of the specialist business team. The information provided would depend upon the enquiry, but typically the enquiry would be dealt with in the same way as proactive contact by Roche with the enquirer (if a non-health professional or professional status unknown) being sent the wallet, 'Survive' guidelines and, for health professionals only, the sales aid and/or drug information pack.

Initial contact with companies was made by telephone. This would sometimes be followed up by a visit.

In conclusion, Roche noted that both in intent and practice, Tamiflu was not promoted to non-health professionals.

PANEL RULING

The Panel noted that the published article which gave rise to this case referred to evidence submitted by an ex-employee of Roche to an employment tribunal. The tribunal had not published its decision when the article was published. Roche submitted that some points had been misreported.

The Panel noted the allegation that the company pressurised its staff to sell Tamiflu to people who were not doctors. The Code covered the promotion of medicines to members of the health professions and appropriate administrative staff (Clause 1.1). Thus POMs could be promoted to persons who were not doctors, such as senior NHS managers and the like, so long as the material or activity was relevant and tailored to the audience and otherwise complied with the Code. POMs could not be promoted to the general public (Clause 22.1).

The Panel noted Roche's submission that the members of the relevant business team would speak to a health professional or the person responsible for continuity planning. Tamiflu would not be promoted to non-health professionals. The 'Process for 1:1 Call Structure' flow chart featured a highlighted box at the top headed 'Guidelines' which stated 'If speaking to a doctor/nurse/medically qualified individual we discuss antivirals/Tamiflu. If speaking to non-medic, we talk generically about supporting their pandemic plan and that we would need to speak to their medical advisor to discuss medical support and POM's' [sic]. The flow chart referred to the provision of materials to support Tamiflu to those companies which did not have antivirals in their pandemic plan. The materials were to be supplied to 'medics only' and thereafter the conversation was terminated. For those companies which had antivirals in their pandemic plan the flow chart continued, discussing, *inter alia*, appropriate prescribing models and options and concluding with an order. It was difficult to see how a conversation with someone who was not medically qualified would fit with this flow chart. The Panel queried whether sufficient instruction in relation to companies without a medically qualified member of staff had been given. A separate flow chart 'Process for Corporate Prospecting' covered general enquiries about a company's position on pandemic

influenza planning. A highlighted box 'Guidelines' at the bottom of this flow chart again stated that 'If speaking to a doctor/nurse/medically qualified individual we discuss antivirals/Tamiflu. If speaking to non-medic, we talk generically about supporting their pandemic plan and that we would need to speak to their medical advisor to discuss medical support'.

The Panel noted Roche's submission about the material supplied to target groups. It was of concern that a sales aid which Roche stated in practice was only supplied to health professionals was certified for use with the business community and occupational health. The Panel also queried whether the flow chart 'Process for Corporate Prospecting' was sufficiently clear about what materials were to be given to who. It referred to sending a 'Letter/Brochure' to relevant persons 'Pharma – Medic, Others – [Business Continuity Manager]/General Manager.' This was followed by a list of approved materials but did not specify which were suitable for non-medically qualified people. The business continuity wallet for example might contain a sales aid if sent to a doctor. The approved letters were not further identified. The Panel noted Roche's submission in this regard. The Panel noted however that the covering letter for the drug information pack discussed Tamiflu in the prevention of influenza. The Panel considered that the instructions in the flow chart 'Process for Corporate Prospecting' regarding the materials' intended audience and in the flow chart 'Process for 1.1 Call Structure' about discussions with non-medically qualified persons were not sufficiently clear. Nonetheless taking all the circumstances into account there was no evidence to show that on the balance of probabilities Roche had actually promoted Tamiflu to a non-health professional as alleged. No breaches of Clauses 9.1 and 2 were ruled.

The article referred, *inter alia*, to the provision of discounts and cash payments on future orders to customers. Roche noted that reference to discounts or cash equivalent rebates had been made in the tribunal proceedings but there was no reference to cash payments. Roche confirmed that it provided customers with rebates in the form of credit notes. The Panel noted that the supplementary information to Clause 18.1 stated that the measures or trade practices relating to prices, margins and discounts which were in regular use by a significant proportion of the pharmaceutical industry on 1 January 1993 were outside the scope of the Code and were excluded from the provision of Clause 18.1 which related *inter alia* to gifts and inducements. Prices, margins and discounts were primarily financial terms. In principle credit notes and discounts which met the requirements of the relevant supplementary information were excluded from the provisions of Clause 18.1. The Panel had no information about the nature of the credit notes provided by Roche. However there was no evidence before the Panel to indicate that inappropriate discounts or cash payments had been made contrary to the provisions of Clause 18.1. Thus no breach of that clause was ruled. The Panel consequently ruled no breach of Clauses 9.1 and 2 on this point.

Complaint received **25 May 2010**

Case completed **5 July 2010**

CASE AUTH/2322/5/10

VOLUNTARY ADMISSION BY ASTRAZENECA

Conduct of representative

AstraZeneca voluntarily admitted breaches of the Code in that a contract representative arranged for a practice nurse at one surgery to undertake a clinical review of chronic obstructive pulmonary disease (COPD) patients at another surgery. The arrangements were not reviewed or approved by AstraZeneca and nor were any documents or records generated in relation to the service.

The Authority's Constitution and Procedure provided that a voluntary admission should be treated as a complaint if it related to potentially serious breaches of the Code or if the company failed to address the matter. That a representative arranged for a clinical review of patients without the company's knowledge was a potentially serious matter and the admission was thus treated as a complaint.

AstraZeneca stated that although the representative had left the employment of the contract sales organisation before the concern about his conduct was raised (and therefore no longer worked for or on behalf of AstraZeneca), it had established the following:

In November 2009 the representative agreed with a practice nurse that that nurse would undertake a clinical review of COPD patients at another local practice and train the resident practice nurse there on findings from the review.

The representative entered into this agreement under his own initiative. He had not been instructed, required, briefed or trained by anyone from AstraZeneca or any other organisation to undertake such an activity.

The representative misleadingly submitted this activity for approval by his AstraZeneca manager, describing it as a speaker's agreement with the nurse. The approval request did not refer to the delivery of clinical patient reviews. The manager challenged the proposed payment (£300) for speaking but the representative implied that that represented fair market value for the nurse in question. Clinical review services were not mentioned by the representative to the manager. The manager approved the request for what he believed was a straightforward educational speaking engagement.

No written agreements existed of any kind between any of the interested parties. Nor were any other documents generated in relation to the service.

The nurse at the practice where the service was to be delivered discussed the service with the GP lead at that practice. The GP believed that he saw a service protocol and subsequently gave verbal approval to his practice nurse for the service to proceed. AstraZeneca did not have a copy of this protocol.

The nurse who delivered the service reviewed 30-40 patients according to standards of good clinical practice. The nurse did not declare to any of the patients that she was being sponsored by AstraZeneca (and nor did the representative request that the nurse make such a declaration).

The verbal agreement between the nurse and representative specified a payment of £20/hour, resulting in a total of approximately £300 for all the hours of service delivered by the nurse. However, AstraZeneca had not paid these monies and would not.

The representative had been comprehensively trained on the requirements of the Code and relevant AstraZeneca policies. He had also passed the ABPI representatives' examination. Despite this training, he initiated unapproved activities without following appropriate AstraZeneca processes and misled AstraZeneca about the nature of those activities. The representative had not maintained a high standard of ethical conduct in the discharge of his duties.

AstraZeneca provided details of some of the corrective actions it had taken both in-house and with the practice where the clinical review was performed.

The detailed response from AstraZeneca is given below.

The Panel noted that without AstraZeneca's knowledge, the representative in question had arranged for a nurse from one general practice to review COPD patients in another practice and train the nurse at the second practice on the findings from the review. The representative had offered to pay the nurse and, in order to get the expenditure approved, had told his manager that the nurse would be 'doing a COPD meeting and discussing how Symbicort fits in for [AstraZeneca]. She will also spend a little time doing some case studies'. When the manager queried the agreed fee of £300 the representative stated that the nurse was very influential within respiratory circles and had spoken for AstraZeneca before. The representative further stated that the nurse knew that £300 did not reflect the usual honoraria for speaking. The manager then agreed to the payment. The fee had not been paid.

The Panel considered that the representative's conduct was wholly unacceptable and, although he had acted on his own initiative and against company policy, AstraZeneca was nonetheless responsible for his actions. The Panel was extremely concerned that there was no way of knowing if the nurse, who had reviewed the COPD patients, had the necessary expertise to perform the task for which the representative had offered to pay. The Panel queried whether, as a result, patients had been put at risk. It appeared that the nurse had undertaken a therapy review service and the involvement of AstraZeneca had not been made clear to patients. No documentation or records of the service had been kept if such materials had been produced.

The Panel considered that the provision of an unapproved, ad hoc medical service by a representative whose role was to promote medicines was unacceptable. A breach of the Code was ruled. The Panel noted that it was clear that materials had either not been produced or not been kept. The GP referred to a protocol which AstraZeneca had not been given. The Panel considered that as no materials had been supplied and given the circumstances it decided that there was not sufficient information to rule a breach with regard to the need for certification and thus no breach of the Code in that regard was ruled.

The Panel did not consider that the representative had maintained a high standard of ethical conduct. A breach of the Code was ruled.

The Panel noted AstraZeneca had known nothing about the clinical review until after the event, the Panel nonetheless considered that high standards had not been maintained. The Panel noted that the requested fee of £300 exceeded AstraZeneca's stated company policy with regard to the recommended payment for a nurse speaker which, for a presentation, typically 1-1½ hours including some preparation, was £150-£250. In the Panel's view a request for a higher than normal honorarium to a nurse not known to the representative's manager as being a local opinion leader should have been more closely scrutinised and should have required the provision of some supporting documentation from the representative. In that regard the Panel requested that AstraZeneca be reminded of the requirements of the Code with regard to the use of consultants. As it was, the expenditure was agreed over the course of two days and four very short emails between the manager and the representative. There appeared to be a lack of management control. High standards had not been maintained. A breach of the Code was ruled which was appealed.

The Panel considered that the representative's conduct, and the lack of control within AstraZeneca which allowed the clinical review to take place, brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled which was appealed.

The Appeal Board noted that the representative at issue had only worked for AstraZeneca for a few months and had left the company in January 2010 following concerns about poor performance including administration issues. AstraZeneca's representatives at the appeal explained that the company first knew about the clinical review in February when the nurse who had carried out the work, and who could no longer contact the representative, contacted the company direct to request payment. The representative's manager had immediately raised the matter and this had prompted an internal investigation which subsequently led to AstraZeneca's voluntary admission.

The Appeal Board noted that AstraZeneca had policies and procedures in place to ensure compliance with the Code and, assuming compliance with those policies and procedures, the representative's manager had, with little resistance, taken the representative's account of the planned speaker meeting at face value. AstraZeneca's representatives at the appeal stated that the manager had no reason to suspect malintent or subterfuge. Nonetheless, the Appeal Board considered that more diligence should have been exercised with regard to the approval of a payment to a speaker that was outwith the company's stated policy.

The Appeal Board considered that the representative's deception of his manager was wholly unacceptable. Although the representative had acted alone in this regard, and contrary to company policy and training, AstraZeneca was nonetheless responsible for his actions. In the Appeal Board's view the manager should have shown much greater scrutiny. High standards had not been maintained. The Appeal Board upheld the Panel's ruling of a breach of the Code. The appeal on this point was thus unsuccessful.
The Appeal Board noted its comments and ruling above and considered that, on balance and given the particular facts of this case, AstraZeneca had not brought discredit upon or reduced confidence in the pharmaceutical industry. The Appeal Board ruled no breach of Clause 2. The appeal on this point was thus successful.

AstraZeneca UK Limited voluntarily admitted breaches of the Code in that a contract representative arranged for a practice nurse at one surgery to undertake a clinical review of chronic obstructive pulmonary disease (COPD) patients at another surgery. The arrangements were not reviewed or approved by AstraZeneca and nor were any documents or records generated in relation to the service.

Paragraph 5.4 of the Constitution and Procedure provided that a voluntary admission should be treated as a complaint if it related to potentially serious breaches of the Code or if the company failed to address the matter. That a representative arranged for a clinical review of patients without the

company's knowledge was a potentially serious matter and the admission was thus treated as a complaint.

COMPLAINT

AstraZeneca stated that the representative in question was employed by a contract sales organisation. Although the representative had left the employment of the contract sales organisation before the concern about his conduct was raised (and therefore no longer worked for or on behalf of AstraZeneca), AstraZeneca had established the following:

In November 2009 the representative, working for AstraZeneca, verbally agreed with a practice nurse that that nurse would undertake a clinical review of COPD patients at another local practice and train the resident practice nurse there on findings from the review.

- The representative entered into this agreement under his own initiative. He had not been instructed, required, briefed or trained by anyone from AstraZeneca or any other organisation to undertake such an activity.

- The representative misleadingly submitted this activity for approval by his AstraZeneca manager, describing it as an agreement with the nurse to deliver an educational speaking engagement. The approval request did not refer to the delivery of clinical patient reviews. The manager challenged the proposed payment (£300) for a speaking engagement but the representative implied that that represented fair market value for the nurse in question. Clinical review services were not mentioned by the representative to the manager. The manager approved the request for what he believed was a straightforward educational speaking engagement.

- Neither the representative nor any other party created a written agreement of any kind. No written agreements existed between AstraZeneca and the nurse or between AstraZeneca and the practice where the service was to be delivered.

- No written material relating to the service was generated by the representative and nor was such material certified. Therefore, AstraZeneca believed there had been a breach of Clauses 14.1 and 18.4 of the Code.

- No documents in relation to this service were generated or kept on record by the company. Therefore, AstraZeneca believed there had been a breach of Clause 18.5.

- The representative told the practice where the service was to be delivered that such a service was being arranged and again, verbally agreed with the nurse at that practice for its delivery.

- The nurse at the practice where the service was to be delivered discussed the service with the GP lead at that practice. The GP believed that he saw a protocol for the service and subsequently gave verbal approval to his practice nurse for the service to proceed. AstraZeneca had not been able to secure a copy of this protocol.

- The nurse who delivered the service reviewed approximately 30 to 40 patients according to standards of good clinical practice. The nurse did not declare to any of the patients that she was being sponsored by AstraZeneca to undertake the review (and nor did the representative request of the nurse that she make such a declaration). Therefore, AstraZeneca believed there had been a breach of Clause 9.10.

- The verbal agreement between the nurse and representative specified a payment of £20/hour, resulting in a total of approximately £300 for all the hours of service delivered by the nurse. However, AstraZeneca had not paid these monies and would not.

The representative had been comprehensively trained by AstraZeneca (and the contract sales organisation) on the requirements of the Code, including those related to medical and educational goods and services, as well as the AstraZeneca External Meetings Policy. He had also passed the ABPI examination for representatives. Despite this training, he initiated unapproved activities without following appropriate AstraZeneca processes and misled AstraZeneca about the nature of those activities. The representative had not maintained a high standard of ethical conduct in the discharge of his duties. Therefore, AstraZeneca believed there had been a breach of Clause 15.2.

AstraZeneca stated that in terms of corrective action, it had contacted the practice where the service was undertaken and fully disclosed this unapproved service to the GP lead there. In particular, the company disclosed the fact that the nurse had not declared AstraZeneca sponsorship to the patients reviewed and nor had AstraZeneca put in place written or verbal requirements for this to occur. AstraZeneca explicitly asked the GP whether further corrective actions were required and was informed not.

AstraZeneca was thoroughly reviewing the representative recruitment and training processes used by the contract sales organisation in question in order to ensure that they met the standards required by AstraZeneca (although AstraZeneca did not rely solely on those processes since representatives supplied by the contract sales organisation were required to undergo the full AstraZeneca Initial Training Course (ITC) and validation).

AstraZeneca stated that it would train all sales personnel, including managers, on the final learnings from this case once it was completed.

Finally, in terms of corrective action AstraZeneca noted that it had submitted this voluntary admission.

AstraZeneca stated that it took compliance with the Code extremely seriously and believed that this was an isolated incident in which a trained contract sales representative initiated an unrequested and unapproved activity and misled his AstraZeneca manager with regard to the nature of that activity. The representative left the employment of the contract sales organisation before the concern was raised and had not worked for or on behalf of AstraZeneca since.

In addition to those clauses cited by AstraZeneca, when writing to inform it that the voluntary admission would be taken up as a complaint, the Authority asked it to comment in relation to the requirements of Clauses 2 and 9.1.

RESPONSE

AstraZeneca explained that the representative was employed by the contract sales organisation as a full-time AstraZeneca representative between April 2009 and January 2010. The representative's services were supplied under the terms of a detailed contract between the companies which included requirements for contract sales organisation to comply with the Code.

As part of his initial training course, the representative received the following comprehensive training from the contract sales organisation and AstraZeneca:

- As part of its training program for representatives, the contract sales organisation trained the representative on the Code in April 2009, and this included specific instruction on Clause 18. The representative passed a written test of his knowledge of the Code at the end of this training.

- This was reinforced by the training in May 2009 by AstraZeneca on the Code, as part of its comprehensive training program for representatives; this also included specific instruction on the requirements of Clause 18.

- The representative was also required to read, acknowledge his compliance with, and pass an examination on his understanding of the AstraZeneca 'UK Pharma Code'. This was a comprehensive AstraZeneca internal policy based on the Code. It covered the AstraZeneca requirements for promotional and non-promotional activities undertaken by representatives and other company personnel, including the requirements for medical and educational goods and services. The representative passed the examination for this policy and acknowledged his compliance with it in May 2009. This policy explicitly stipulated that 'Materials relating to the provision of medical and educational goods and services … must be examined by the local Nominated Signatories and certified as acceptable under all applicable internal and external codes, laws and regulations'. The representative did not submit nor receive any such approval from any AstraZeneca or contract sales organisation personnel.

- The representative was also required to read and acknowledge his compliance with the AstraZeneca Global Code of Conduct, and he did so in May 2009. This was an internal code which required all employees to maintain high standards of ethical conduct in all their activities.

- The representative had passed the ABPI examination for representatives.

Despite all the above training, the representative initiated activities that had not been reviewed or approved through appropriate AstraZeneca processes and misled his AstraZeneca manager about the nature of those activities. As required by company guidance regarding payment of speakers' fees to health professionals, the representative requested approval from his manager for planned costs of £350 (comprised of a £300 fee to the nurse and £50 budgeted for subsistence and expenses) using the AstraZeneca electronic territory management system. However, the request was presented as approval of a proposed cost for the nurse to deliver an educational meeting ('speaker meeting'). There was no indication in the approval request, either explicit or implicit, that the proposal included delivery of patient clinical review services.

In the course of email correspondence, the manager queried the justification for the level of the proposed honorarium (even though it was potentially within AstraZeneca guidance regarding payment of speakers' fees). The representative responded with a justification based on the fair market value of the nurse. The representative, again, did not use this opportunity to declare the true nature of the proposed activity to his manager and continued to present the activity as a speaker meeting. The manager then approved this proposed fee, in the reasonable belief that it was for an educational speaker meeting. AstraZeneca noted that once the circumstances of this activity were investigated and established, the company did not, and would not, pay the fee.

AstraZeneca stated that the representative appeared to have willfully misled the manager and such isolated, deliberate acts could not, in every instance, be reasonably prevented by policies, processes or managerial oversight even where these were robust.

AstraZeneca encouraged and set out clear internal processes for all employees to raise concerns relating to compliance. In this case, concerns were raised by the representative's manager when he was contacted by the nurse requesting payment for

this clinical service (after the representative had left employment with the contract sales organisation and AstraZeneca).

In response to the concerns raised, a thorough investigation was undertaken to establish the facts and AstraZeneca noted the corrective actions it had taken as detailed above.

AstraZeneca considered that the representative was comprehensively trained on the Code as part of established and robust company training programs and that reasonable control was exercised over their activity, as set out above.

When a potential compliance concern was raised internally, AstraZeneca immediately undertook a thorough investigation and took internal and external corrective actions as set out above because it took compliance with the Code extremely seriously. Therefore, AstraZeneca denied a breach of Clause 9.1.

The representative appeared to have acted in a willfully misleading manner and in contravention of his training. AstraZeneca believed this was an isolated and unforeseeable individual act which was identified and acted upon internally. Therefore, AstraZeneca did not consider there had been a breach of Clause 2.

PANEL RULING

The Panel noted that without AstraZeneca's knowledge, the representative in question had arranged for a nurse from one general practice to review COPD patients in another practice and train the nurse at the second practice on the findings from the review. The representative had offered to pay the nurse and, in order to get the expenditure approved, had told his manager that the nurse would be 'doing a COPD meeting and discussing how Symbicort fits in for [AstraZeneca]. She will also spend a little time doing some case studies'. When the manager queried the agreed fee of £300 the representative stated that the nurse was very influential within respiratory circles and had spoken for AstraZeneca before. The representative further stated that the nurse knew that £300 did not reflect the usual honoraria for speaking. The manager then agreed to the payment. The fee had not been paid.

The Panel considered that the representative's conduct was wholly unacceptable and, although he had acted on his own initiative and against company policy, AstraZeneca was nonetheless responsible for his actions. The Panel was extremely concerned that there was no way of knowing if the nurse, who had reviewed the COPD patients, had the necessary expertise to perform the task for which the representative had offered to pay. The Panel queried whether, as a result, patients had been put at risk. It appeared that the nurse had undertaken a therapy review service and the involvement of AstraZeneca had not been made clear to patients. No documentation or records of the service had been kept if such materials had been produced.

The Panel considered that the provision of an unapproved, ad hoc medical service by a representative whose role was to promote medicines was unacceptable. A breach of Clause 18.4 was ruled. The Panel noted that AstraZeneca had acknowledged a breach of Clause 14.1 as materials had not been certified. Clause 14.1 related to promotional material and clearly a medical or educational good or service should not be promotional. Clause 14.3 required certification of materials for patients or health professionals relating to the provision of medical and educational goods and services including relevant internal company instructions. AstraZeneca had not been asked to respond in relation to the requirements of Clause 14.3. It was clear that materials had either not been produced or not been kept. The GP referred to a protocol which AstraZeneca had not been given. The Panel considered that as no materials had been supplied and given the circumstances it decided that there was not sufficient information to rule a breach of Clause 14.1 and thus ruled no breach.

The Panel noted its ruling of a breach of Clause 18.4, it thus considered that the matter was not covered by Clause 18.5 which referred to activities not otherwise covered by the Code. No breach of Clause 18.5 was ruled.

The Panel did not consider that the representative had maintained a high standard of ethical conduct. A breach of Clause 15.2 was ruled.

The Panel noted that AstraZeneca had acknowledged the breaches of the Code as detailed above. The company had, in addition, been asked to consider the requirements of Clauses 9.1 and 2 of the Code. Although noting that AstraZeneca had known nothing about the clinical review until after the event, the Panel nonetheless considered that high standards had not been maintained. The Panel noted that the requested fee of £300 exceeded the recommended payment for a nurse speaker as stated in AstraZeneca's External Meetings Policy document. According to the company's stated policy, nurse speakers (for a presentation, typically 1-11/2 hours including some preparation) were to be paid £150-£250. In the Panel's view a request for a higher than normal honorarium to a nurse not known to the representative's manager as being a local opinion leader should have been more closely scrutinised and should have required the provision of some supporting documentation from the representative. In that regard the Panel requested that AstraZeneca be reminded of the requirements of Clause 20. As it was, the expenditure was agreed over the course of two days and four very short emails between the manager and the representative. There appeared to be a lack of management control. High standards had not been maintained. A breach of Clause 9.1 was ruled. This ruling was appealed.

The Panel considered that the representative's conduct, and the lack of control within AstraZeneca which allowed the clinical review to take place, brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled. This ruling was appealed.

APPEAL BY ASTRAZENECA

AstraZeneca reiterated that it took adherence with the Code extremely seriously; it had created a culture that encouraged employees to internally raise compliance concerns secure in the knowledge that such concerns would be investigated and addressed appropriately. Consistent with that culture, this compliance issue was internally raised in response to which AstraZeneca conducted a thorough investigation and submitted a voluntary admission.

AstraZeneca submitted that with regard to the ruling of a breach of Clause 9.1, the Panel noted that AstraZeneca had known nothing about the clinical review until after the event but it nonetheless considered that high standards had not been maintained. This conclusion was reached on the basis that the proposed fee to the nurse of £300 exceeded the recommended guidance for a nurse speaker in the AstraZeneca External Meetings Policy. It was the Panel's view that such a proposal should have been more closely scrutinized and that there appeared to be a lack of management control. The Panel stated that as it was, the expenditure was agreed over the course of two days and four very short emails between the manager and the representative. In responding to these points, AstraZeneca reiterated the actions that the manager took to exercise control over the proposed activity.

AstraZeneca noted that in November 2009, the representative submitted the proposed educational meeting for approval by his manager, entering the details into AstraZeneca electronic territory management system. A printout of those details, previously provided, clearly identified the proposed activity as a 'Speaker Meeting' to take place in November 2009.

AstraZeneca provided a 'screenshot' of the information the manager would have seen on his computer screen when viewing the details of the proposed activity in the electronic territory management system. This clearly showed that under the heading 'Event Type', the representative had specified 'Speaker Meeting'. Under the heading 'Objective', he had stated 'Further account objectives' and under 'Recruitment Criteria' (ie nature of delegates), he had stated 'Drs and nurses'. He had also indicated that the proposed number of delegates was 5 and that the average cost per head would be £70. The field requiring approval by the manager was headed 'Meeting Approved by' and the optional field for 'Meeting Notes' was left blank. Therefore, it appeared to the manager that this proposed activity, for their approval, was purely a speaker meeting.

Despite the apparently straightforward nature of the representative's proposal the manager challenged the request for approval, as shown in the email exchange previously provided. The manager challenged the level of expenditure by asking 'Is [nurse] a very well respected KOL [key opinion leader] as this seems a large honoraria for a first meeting or has she spoken for us before?' In response to this challenge, the representative stated '[Nurse] is very influential within respiratory circles and she has spoken for us in the past. This is higher than the usual fee as a one off as she is doing the meeting then spending some time on top doing some COPD case studies to really bring the meeting content to life for us'. With this information before them, AstraZeneca did not believe that it was unreasonable for the manager to consider that he was approving fees for a speaker with a high market value and that the speaker would need to spend a significant amount of time (above and beyond that needed for an average speaker meeting) preparing case studies specifically for this meeting. Based on such consideration, AstraZeneca did not believe it was unreasonable for the manager to approve a fee that was a little above the guidance in the AstraZeneca External Meetings Policy (ie they approved £300 rather than £250), as compensation for the significant amount of extra time that would have been reasonably expected to be required to prepare new case studies specifically for this meeting. AstraZeneca therefore submitted that the proposed fee was not inconsistent with its External Meetings Policy.

AstraZeneca submitted that the manager had no reason to consider that the information supplied by the representative wholly misrepresented the nature of the activity type. Therefore, and for the reasons described above, AstraZeneca submitted that the manager acted in a reasonable and proportionate manner; the company did not agree that there was a lack of management control and nor therefore, that there had been a breach of Clause 9.1.

AstraZeneca noted that with regard to the ruling of a breach of Clause 2, the Panel considered '… that the representative's conduct, and the lack of control within AstraZeneca which allowed the clinical review to take place, brought discredit upon and reduced confidence in the pharmaceutical industry'.

AstraZeneca agreed that the representative in this instance did not maintain a high standard of ethical conduct and did not comply with all relevant requirements of the Code. This was despite the extensive training he received and acknowledged on the Code and company policy from both AstraZeneca and the contract sales organization. Accordingly, AstraZeneca had accepted a ruling of a breach of Clause 15.2. However, for the detailed reasons set out below, AstraZeneca did not agree that there had been a lack of control.

AstraZeneca submitted that it had robust contracts

and detailed policies in place that governed the actions of representatives and the processes and systems to ensure that these were implemented. The company had a dedicated Learning & Development department that created and delivered extensive mandatory training to all new representatives (including contract sales representatives) on the technical aspects of products they were required to promote, how they were to promote them and the compliance requirements related to their role, as well as the requirements of the Code (including the requirements of Clause 18). The representative in question underwent this training in April 2009.

All company personnel and contracted sales personnel were required to demonstrate a thorough understanding of the 'AstraZeneca UK Pharma Code' and to pass a test assessing their knowledge and understanding of it. They were then required to record their acknowledgement that they understood, and would comply with this code. This code was an extensive document based on the ABPI Code and provided a great deal of specific guidance on the activities of personnel including representatives. It covered the AstraZeneca requirements for promotional and non-promotional activities undertaken by representatives and other company personnel, including the requirements for medical and educational goods and services. The representative passed the examination for this policy and acknowledged his compliance with it in May 2009. The policy explicitly stipulated that 'Materials relating to the provision of medical and educational goods and services…must be examined by the local Nominated Signatories and certified as acceptable under all applicable internal and external codes, laws and regulations'. The representative in this case did not submit nor receive any such approval from anyone in AstraZeneca or the contract sales organisation.

All AstraZeneca personnel and contract sales personnel were required to annually read and acknowledge their understanding and compliance with the 'AstraZeneca Global Code of Conduct'. This overarching AstraZeneca code required all employees and third party service providers (including contracted sales personnel) to act with integrity and maintain a high standard of ethical conduct at all times. The representative in this case acknowledged his compliance with this code in May 2009.

AstraZeneca had robust contractual provisions in place with all of its contract sales organizations including the one that had employed the representative in question. The contract sales organisation and its employees were obliged under the terms of the contract to carry out any and all services on behalf of AstraZeneca in compliance with the Code, and only through sales representatives who were appropriately trained, had passed the validation and had the relevant skills, knowledge, qualification and experience to undertake their tasks in a professional and competent manner. Furthermore, AstraZeneca's contracts obligated the contract sales organisation to promptly inform AstraZeneca of any circumstances it became aware of (for whatever reason) regarding any of its employees that made that person unsuitable to provide services on behalf of AstraZeneca. The representative in this case had passed the ABPI examination for representatives in 2006, had undergone initial training on the Code by the contract sales organisation in April 2009 (including the requirements of Clause 18) and had passed a written test demonstrating his knowledge of the Code at the end of this training. This training was in addition to the training administered separately by AstraZeneca on the Code and the requirements of Clause 18, referred to above.

AstraZeneca submitted that all of its representatives were required to attend a quarterly local training meeting on the Code, delivered by specially trained members of their regional sales management during which recent PMCPA cases relevant to the field and other topical matters related to the Code were presented and discussed. The representative in this case attended such a meeting during his seven months of active service with AstraZeneca.

All representatives were trained in detail on the AstraZeneca electronic territory management system which was a comprehensive resource for recording calls on health practitioners and for planning, recording and approving proposed educational or promotional meetings. There was no process available within that system for the approval of patient review services. The training representatives received on the approval of meetings using the system did not refer to patient review services in any way, nor could there be any misunderstanding that the meetings approval process could be used for the approval of patient review services. The representative in this case underwent detailed training on the system in April 2009.

AstraZeneca submitted that it strongly encouraged its employees and third party service providers to raise any compliance concerns they had and provided a process and independent resource for doing this. Employees might raise issues, through a number of routes, including an independently administered telephone line and web-site. This was a key control mechanism, above and beyond that required by the Code.

AstraZeneca re-emphasised that this compliance issue was initially brought to its attention as a result of an internally raised concern. When contacted by AstraZeneca, the GP in the practice where the patient reviews took place did not raise a complaint or request any further corrective actions. The fact that the compliance issue was raised internally was in keeping with the culture at AstraZeneca that encouraged employees to raise such concerns in the knowledge that they would be investigated and addressed appropriately. AstraZeneca treated this case with the seriousness it merited when it was

raised and conducted a thorough investigation and corrective actions. In that regard AstraZeneca noted that it had submitted a voluntary admission to the PMCPA. The company had also contacted the practice where this service was undertaken and fully disclosed to the GP lead there that the patient review service had not been arranged according to appropriate AstraZeneca processes and that written agreements had not been put in place by AstraZeneca with the practice. AstraZeneca had disclosed the fact that the nurse had not declared AstraZeneca support to the patients reviewed. AstraZeneca explicitly asked the GP whether he required further actions of a corrective nature of any kind and was informed that he did not. In addition AstraZeneca had undertaken a thorough review of the representative training processes used by the contract sales organisation in question in order to ensure it met the standards required by AstraZeneca. AstraZeneca would train all sales personnel, including managers, on the final learnings from this case once it was completed.

AstraZeneca fully understood that all companies had a responsibility to have in place adequate procedures designed to prevent persons from undertaking activities in breach of the Code. AstraZeneca submitted that it had in place such procedures and controls and that these were over and above the minimum standard required and had applied them in this case. However, despite the robust contract, systems/processes and training, the representative appeared to have acted on his own volition to proactively circumvent these controls and procedures without AstraZeneca's instruction, knowledge or approval. AstraZeneca did not agree that such actions or omissions of the representative in this case indicated a lack of adequate control.

AstraZeneca re-emphasized that it took the positive decision to submit a voluntary admission - such openness and transparency would ultimately enhance the reputation of the industry and bring credit upon it rather than the converse.

AstraZeneca submitted that there had not been a lack of control nor had this matter brought discredit to or reduced confidence in the industry. Therefore, AstraZeneca denied a breach of Clause 2.

In summary, AstraZeneca submitted that it had in place the reasonable controls and more, expected of a pharmaceutical company and applied those controls in this case as set out above and that the circumstances of this matter were not such as to warrant a ruling of breaches of Clauses 2 and 9.1.

APPEAL BOARD RULING

The Appeal Board noted that the representative at issue had only worked for AstraZeneca for a few months. The representative had left the company in January 2010 following concerns about poor performance including administration issues. AstraZeneca's representatives at the appeal explained that the company first knew about the clinical review in February when the nurse who had carried out the work, and who could no longer contact the representative, contacted the company direct to request payment. The representative's manager had immediately raised the matter and this had prompted an internal investigation which subsequently led to AstraZeneca's voluntary admission.

The Appeal Board noted that AstraZeneca had policies and procedures in place to ensure compliance with the Code and, assuming compliance with those policies and procedures, the representative's manager had, with little resistance, taken the representative's account of the planned speaker meeting at face value. AstraZeneca's representatives at the appeal stated that the manager had no reason to suspect malintent or subterfuge. Nonetheless, the Appeal Board considered that more diligence should have been exercised with regard to the approval of a payment to a speaker that was outwith the company's stated policy.

The Appeal Board considered that the representative's deception of his manager was wholly unacceptable. Although the representative had acted alone in this regard, and contrary to company policy and training, AstraZeneca was nonetheless responsible for the representative's actions. In the Appeal Board's view the manager should have shown much greater scrutiny. High standards had not been maintained. The Appeal Board upheld the Panel's ruling of a breach of Clause 9.1. The appeal on this point was thus unsuccessful.

The Appeal Board noted its comments and ruling above and considered that, on balance and given the particular facts of this case, AstraZeneca had not brought discredit upon or reduced confidence in the pharmaceutical industry. The Appeal Board ruled no breach of Clause 2. The appeal on this point was thus successful.

Complaint received **25 May 2010**

Case completed **6 August 2010**

CASE AUTH/2324/6/10

PFIZER v JOHNSON & JOHNSON

Promotion of Nicorette

Pfizer complained about a slide entitled 'Stapleton: Combination Success Rates at 4 weeks' within a Nicorette (nicotine transdermal patch) presentation issued by Johnson & Johnson entitled 'Hitting "Hard to Reach Targets" with High Dose & Combination NRT [nicotine replacement therapy]'. Pfizer produced Champix (varenicline).

The slide in question was referenced to Stapleton *et al* (2008) (the published paper was dated 2007). The first bullet point read, 'Evaluation of consecutive routine cases before and after the introduction of varenicline (N=412)' and appeared above a bar chart headed 'Abstinence rates at 4 weeks'. The bar chart stated to be adapted from Stapleton *et al* (2008) compared the percentage abstinence rates of combination NRT (66.3%) with varenicline (72.1%). Between the bars appeared 'ns*'. Two bullet points beneath the bar chart read '2 out of 3 smokers on combination NRT were abstinent at 4 weeks' and 'No statistically significant difference between combination NRT and varenicline*'. The two asterisks led the reader to a small footnote at the bottom of the slide which read 'Evaluation not designed to detect a difference between combination NRT and varenicline'.

Pfizer noted that Stapleton *et al* discussed the short-term smoking cessation rates for varenicline, single NRT and combination NRT. The authors concluded that '… we observed little difference between the efficacy of varenicline and combination NRT therapy …' they also stated '… although this evaluation was not designed with adequate statistical power to test this'. Although a small footnote to this effect appeared on the slide, the Code stated that 'In general, claims should not be qualified by the use of footnotes and the like'. Pfizer considered that overall the slide implied that there was no significant difference between varenicline and combination NRT smoking cessation therapies even though the authors explicitly stated that the study was not statistically powered to detect this. Johnson & Johnson argued that the observation of 'no statistically significant difference between NRT and varenicline' was acceptable as a standalone claim and presumably therefore did not require further clarification or qualification. Pfizer contested this assertion.

Pfizer further submitted that the slide clearly represented an attempt to mislead the audience as to the meaning of this result, otherwise why show it at all if the only thing to be demonstrated was that a study which was not designed or powered to show any difference did, indeed, fail to show any difference? It was clearly an attempt to lead the audience to believe that there was no difference in efficacy between varenicline and combination NRT treatment, something which this study was not designed to, and did not, demonstrate.

Pfizer was also concerned that the slide failed to mention that the aforementioned observation was not the primary endpoint of Stapleton *et al*. The authors stated that 'The results suggest that, with routine psychological and behavioural group support, varenicline is more effective than NRT in aiding short-term smoking cessation'. Due to this omission the slide did not fully and accurately reflect the authors' concluding views.

As a result, the slide was misleading regarding the design and results of the study and in particular the details of equivalent efficacy for combination NRT and varenicline in short-term smoking cessation.

The detailed response from Johnson & Johnson is given below.

The Panel noted that Stapleton *et al* compared the effectiveness of varenicline with NRT for smoking cessation and evaluated the safety and effectiveness of varenicline in people with mental illness. The authors stated that 'Varenicline was significantly more effective than single-product NRT therapy and increased cessation rates by about 14% … However, there was no evidence of a difference in success rates between varenicline and combination NRT'. In the discussion section the authors further stated that 'The results suggest that, with routine psychological and behavioural group support, varenicline is more effective than NRT in aiding short-term smoking cessation' and 'Interestingly, we observed little difference between the efficacy of varenicline and combination NRT therapy, although this evaluation was not designed with adequate statistical power to test this'. The authors concluded that 'In this setting and with group support varenicline appears to improve success rates over those achieved with NRT …'.

The Panel noted that the slide in question was part of a presentation about high dose and combination NRT in hard to reach targets. The Panel noted Johnson & Johnson's submission that the data at issue was important and highly relevant to those working in smoking cessation. It was currently the only published data comparing varenicline and combination NRT. Nonetheless the presentation of such data had to comply with the Code. The information had to be sufficiently complete such as to allow clinicians to form their own opinion of the therapeutic value of the data presented.

In the Panel's view the design and content of the

slide implied that Stapleton *et al* was powered to detect a difference between varenicline and combination NRT and that was not so. The Panel considered that the footnote was insufficient to negate the misleading impression about the validity of the comparison and the power of the study. The slide was misleading in this regard as alleged; high standards had not been maintained. Breaches of the Code were ruled.

The Panel noted that the presentation discussed high dose and combination NRT in hard to reach targets. The slide in question presented the combination NRT data vs varenicline. The Panel did not consider that the slide was misleading because it omitted reference to other outcomes from Stapleton *et al* as alleged. No breach of the Code was ruled.

Pfizer Limited complained about a slide entitled 'Stapleton: Combination Success Rates at 4 weeks' within a Nicorette (nicotine transdermal patch) presentation issued by Johnson & Johnson Limited and entitled 'Hitting "Hard to Reach Targets" with High Dose & Combination NRT [nicotine replacement therapy]' (ref 05607). Pfizer produced Champix (varenicline). Inter-company dialogue had failed to resolve the matter.

The slide was referenced to Stapleton *et al* (2008) (the published paper was dated 2007). The first bullet point read, 'Evaluation of consecutive routine cases before and after the introduction of varenicline (N=412)' and appeared above a bar chart headed 'Abstinence rates at 4 weeks'. The bar chart compared the percentage abstinence rates of combination NRT (66.3%) with varenicline (72.1%). Between the bars appeared 'ns*'. It was stated that the bar chart was adapted from Stapleton *et al*. Two bullet points beneath the bar chart read '2 out of 3 smokers on combination NRT were abstinent at 4 weeks' and 'No statistically significant difference between combination NRT and varenicline*'. The two asterisks led the reader to a small footnote at the bottom of the slide, 'Evaluation not designed to detect a difference between combination NRT and varenicline'.

COMPLAINT

Pfizer noted that Stapleton *et al* discussed the short-term smoking cessation rates for varenicline, single NRT and combination NRT. The slide included the claim 'No statistically significant difference between combination NRT and varenicline'. While Stapleton *et al* '… observed little difference between the efficacy of varenicline and combination NRT therapy …' the authors also stated '… although this evaluation was not designed with adequate statistical power to test this'. Although a small footnote to this effect appeared at the bottom of the slide, the supplementary information to Clause 7 stated that 'In general, claims should not be qualified by the use of footnotes and the like'. Pfizer considered that overall the slide implied that there was no significant difference between varenicline and combination NRT smoking cessation therapies even though the authors explicitly stated that the study was not statistically powered to detect this. Johnson & Johnson argued that the observation of 'no statistically significant difference between NRT and varenicline' was acceptable as a standalone claim and presumably therefore did not require further clarification or qualification. Pfizer contested this assertion.

Pfizer further submitted that the slide clearly represented an attempt to mislead the audience as to the meaning of this result, otherwise why show it at all if the only thing to be demonstrated was that a study which was not designed or powered to show any difference did, indeed, fail to show any difference? Pfizer did not consider it was credible that this was the message that Johnson & Johnson wished to convey to its audience. It was clearly an attempt to lead the audience to believe that there was no difference in efficacy between varenicline and combination NRT treatment, something which this study was not designed to, and did not, demonstrate.

Pfizer was also concerned that the slide failed to mention that the aforementioned observation was not the primary endpoint of Stapleton *et al*. The authors stated that 'The results suggest that, with routine psychological and behavioural group support, varenicline is more effective than NRT in aiding short-term smoking cessation'. Due to this omission the slide did not fully and accurately reflect the authors' concluding views.

As a result, the slide was misleading regarding the design and results of the study and in particular the details of equivalent efficacy for combination NRT and varenicline in short-term smoking cessation. Pfizer alleged that the presentation was in breach of Clauses 7.2 and 7.8 of the Code and thus also Clause 9.1.

RESPONSE

Johnson & Johnson stated that the purpose of the presentation was to consider how treatment with high dose NRT could help health professionals, working in smoking cessation, achieve their challenging abstinence targets. Two key areas covered in the presentation were the established benefits of a high dose 16 hour patch compared with standard dose 16 hour patch (25mg vs 15mg) and the benefits of treatment with combination NRT vs monotherapy. Combination NRT usually involved the patient applying a patch to provide baseline nicotine levels and the use of an acute dosage form, as required, to relieve so called 'breakthrough' cravings. This method of treatment had been endorsed by the National Institute for health and Clinical Excellence (NICE), Action on Smoking and Health (ASH) and the Committee on Safety of Medicines (CHM).

The slide in question related to combination NRT usage. More specifically, the slide showed the

absolute 4 week abstinence rates, for varenicline and NRT combination therapy from Stapleton *et al*.

Stapleton *et al* compared the efficacy of varenicline and NRT in smoking cessation and evaluated the safety and efficacy of varenicline in people with mental illness. The study was conducted in an NHS tobacco dependence clinic in London and comprised an evaluation of cases before and after the introduction of varenicline. Patients receiving routine care (N=412) were included in the study and 4 week carbon monoxide verified abstinence rates were measured. The study also measured severity of withdrawal symptoms, incidence and severity of adverse drug symptoms, cost per patient treated and cost per successful quitter. In addition to abstinence rates for varenicline vs all NRT, the authors considered the comparative efficacy of varenicline vs single and combination NRT treatment.

The study demonstrated that cessation rates were higher with varenicline than all NRT (odds ratio = 1.70, 95% confidence interval = 1.09-2.67). However, the comparison between varenicline and combination NRT therapy showed '.... no evidence of a difference in success rates between varenicline and combination NRT (OR for CO-verified abstinence = 1.32, 95% CI=0.76-2.27 and OR for DH self-reported abstinence=1.38, 95% CI=0.76-2.52)'. In the discussion section of the paper, the authors stated '... this evaluation was not designed with adequate statistical power to test this'. The study was published in a peer reviewed journal.

Johnson & Johnson believed the results of Stapleton *et al* were of real importance to health professionals as this was the only published study which assessed the effect of combination NRT treatment in a 'real life' setting. It was also the only available study to have reviewed and compared the efficacy of varenicline and NRT combination treatment. Johnson & Johnson was of the strong view that this data provided those working in the field of smoking cessation with important and highly relevant information.

Both combination NRT therapy and varenicline were effective treatments for smoking cessation; both were commonly prescribed and therefore health professionals often had to decide which of the two to prescribe. The frequent use of combination NRT was illustrated in the study as 41% of patients who opted for NRT used a combination of more than one NRT product. Therefore, if choosing between these two treatments, it was important that the prescriber was aware of all relevant data. In order to help inform this decision, Johnson & Johnson submitted it was important to include the absolute efficacy rates for both treatments.

Johnson & Johnson took great care to ensure that the slide was not misleading in any way. The comparison between varenicline and NRT combination therapy was valid and had been made in the publication. Indeed, the slide simply reflected the comparison as presented by the authors. The bar chart was clearly presented and the bars annotated, in large font, with the absolute abstinence rates for the two groups. In fact the figures actually showed that the varenicline subjects achieved a numerically superior quit rate compared with those patients receiving combination NRT (72.1% vs 66.3% respectively). However, this difference was not statistically significant so the bar chart had been clearly labelled as 'ns'. The bullet point below the bar chart reinforced this fact.

It was entirely appropriate when presenting data in a bar chart to indicate whether or not there was a statistically significant difference between the treatments portrayed; not to do so risked giving a false impression. By providing both the raw data, as well as the statement in the chart and below the chart on the statistical significance, the prescriber was given all the relevant information on this comparison.

Johnson & Johnson strongly objected to Pfizer's allegation that it had attempted to mislead the audience as to the meaning of this result, '…otherwise why show it at all if the only thing to be demonstrated is that a study which was not designed or powered to show any difference did indeed fail to show any difference'. Johnson & Johnson acknowledged that absence of evidence was not the same as evidence of absence. However, it had taken great care to ensure that it had reflected accurately the absolute abstinence rates together with the statistical comparison conducted by the authors.

Johnson & Johnson's intention when developing this slide was to ensure that all relevant information was communicated unambiguously in order that prescribers could make an informed decision. The slide was headed 'Stapleton: Combination Success Rates at 4 weeks' and the bar chart provided the absolute quit rates from the study for both varenicline and combination NRT. These absolute quit rates on their own demonstrated that both combination NRT therapy and varenicline were effective treatments in smoking cessation, irrespective of any comparison between the two. This in itself was an important reason for presenting the data.

Although, as discussed in the publication, the study was not designed with adequate statistical power to detect a difference between combination NRT therapy and varenicline, the authors obviously felt this analysis to be of importance. Indeed, they conducted statistical tests to show that there was no evidence of a difference in success rates between varenicline and combination NRT (OR for CO-verified abstinence =1.32, 95%CI=0.76-2.27 and OR for DH self-report abstinence =1.38, 95% CI=0.76-2.52).

The slide was simply intended to reflect the authors' findings ie that no significant difference was detected between treatments. There was no attempt

to claim that combination NRT was superior or even equivalent to varenicline. The statement that the study did not detect a statistically significant difference between the treatments was absolutely true and could stand alone without further substantiation. However, to ensure absolute clarity regarding the nature of the data, Johnson & Johnson included the additional information about the statistical power of the study as a footnote. It would be inappropriate to use a footnote to correct a false impression. However, Johnson & Johnson did not believe that such an impression had been created. Johnson & Johnson was extremely careful to ensure that all relevant data had been presented in an accurate, balanced, fair, objective, and unambiguous way, based on an up-to-date evaluation of all the evidence. It had also been careful to ensure that all relevant information was reflected clearly. Johnson & Johnson did not believe that the footnote qualified the claim or corrected a wrong impression as suggested by Pfizer, but rather that it provided further useful information about the nature of the data. Johnson & Johnson noted that Pfizer had not provided any data to suggest that varenicline was superior in efficacy to combination NRT therapy.

In summary, Johnson & Johnson believed that the key messages communicated by the slide in question were that both varenicline and NRT combination therapy showed good overall efficacy and that Stapleton *et al* did not provide any evidence that varenicline and NRT combination therapy differed in terms of efficacy. The slide did not give a misleading impression that there was no difference in efficacy between varenicline and combination NRT. On the contrary, it faithfully presented the raw data from the study as well as the authors' conclusions on the comparison between varenicline and combination NRT therapy. The statement that there was 'no statistical difference between combination NRT and varenicline' made it clear that there was no evidence of a difference between treatments in this study, not that the treatments were equivalent. Johnson & Johnson believed that prescribers would understand this. In addition, this information was highly relevant as it was currently the only published data comparing varenicline and combination NRT.

Johnson & Johnson did not believe that the slide was misleading and therefore did not believe that it had breached Clause 7.2 as alleged.

In relation to the allegation that '... the slide failed to mention that the aforementioned observation was not the primary endpoint of Stapleton *et al*', Johnson & Johnson stated that the Code did not require that the primary efficacy endpoints of studies were always provided and it believed that it was acceptable to make comparisons using non-primary endpoints as long as the comparison was justified. In the context of a presentation on high dose NRT, there would be no sense in including the primary endpoint data relating to the comparison between mostly standard dose NRT and varenicline as that was not the subject of the presentation. Johnson & Johnson was not aware of any Code requirement to specify if data cited related to a secondary endpoint.

Johnson & Johnson noted Pfizer's allegation that due to this omission the slide did not fully and accurately reflect the concluding views of the authors. The authors made a number of other conclusions which, although no doubt of general interest, were not relevant to a presentation on NRT combination therapy. There was no obligation under the Code to reflect all the views of the authors of a study from which data was taken. However, the authors' conclusion relevant to combination NRT therapy was accurately reflected in the slide ie '… we observed little difference between the efficacy of varenicline and combination NRT therapy'.

It was entirely justified to present this data on combination NRT vs varenicline in the section of the presentation relating to combination NRT usage. Furthermore, there was no requirement under the Code to specify that the data presented was not the primary endpoint of the study.

Johnson & Johnson disagreed with Pfizer's assertion that the slide was in breach of Clause 7.8. Indeed the bar chart accurately presented the data from Stapleton *et al* and it was clear that it had been adapted from this study. Relevant details were included such as the patient numbers, nature of the cases and the frequency of the background support provided. The absolute quit rates for both varenicline and combination NRT were accurately represented and the quit rates were given within the bars. This allowed the prescriber to see clearly that the quit rates were numerically higher for varenicline. As the authors had conducted statistical significance testing, the fact that the comparison was not significant was reflected in the bar chart as 'ns'.

Johnson & Johnson believed the statement that there was no statistically significant difference between combination NRT and varenicline was acceptable as a standalone statement. However, to ensure that all relevant information was provided, it included a footnote explaining that the trial was not designed to detect a difference between treatments.

Based on the arguments above, Johnson & Johnson did not believe that it had breached Clauses 7.2 and 7.8.

Johnson & Johnson denied Pfizer's allegation that it had failed to maintain high standards. Johnson & Johnson believed that the presentation overall provided health professionals with useful and objective information on a fast developing area within smoking cessation. Moreover, the slide in question was based on robust data from a peer reviewed journal and was presented in a way as to ensure that prescribers had all relevant information to enable them to properly interpret the data.

Johnson & Johnson did not accept that the slide breached Clause 9.1.

PANEL RULING

The Panel noted that Stapleton *et al* compared the effectiveness of varenicline with NRT for smoking cessation and evaluated the safety and effectiveness of varenicline in people with mental illness. The authors stated that 'Varenicline was significantly more effective than single-product NRT therapy and increased cessation rates by about 14% … However, there was no evidence of a difference in success rates between varenicline and combination NRT'. In the discussion section the authors further stated 'The results suggest that, with routine psychological and behavioural group support, varenicline is more effective than NRT in aiding short-term smoking cessation' and 'Interestingly, we observed little difference between the efficacy of varenicline and combination NRT therapy, although this evaluation was not designed with adequate statistical power to test this'. The authors concluded that 'In this setting and with group support varenicline appears to improve success rates over those achieved with NRT …'.

The Panel noted that the slide in question was part of a presentation which examined high dose and combination NRT in hard to reach targets. The Panel noted Johnson & Johnson's submission that the data at issue was important and highly relevant to those working in smoking cessation. It was currently the only published data comparing varenicline and combination NRT. Nonetheless the presentation of such data had to comply with the Code. The information had to be sufficiently complete such as to allow clinicians to form their own opinion of the therapeutic value of the data presented.

In the Panel's view the design and content of the slide implied that Stapleton *et al* was powered to detect a difference between varencline and combination NRT and that was not so. The prominent heading 'Stapleton: Combination Success Rates at 4 weeks' introduced the comparison at issue and gave the impression that the study was adequately powered. Similarly the presentation of the data in the bar chart and the statement 'ns' reinforced the misleading impression that the study had sufficient power to compare varenicline with combination NRT.

The Panel noted that the supplementary information to Clause 7 stated, *inter alia*, 'In general claims should not be qualified by the use of footnotes and the like'. The footnote was insufficient to negate the misleading impression about the validity of the comparison and the power of the study. The slide was misleading in this regard as alleged. Breaches of Clauses 7.2 and 7.8 were ruled. High standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel noted that the presentation discussed high dose and combination NRT in hard to reach targets. The slide in question presented the combination NRT data vs varenicline. The Panel did not consider the slide in question misleading because it omitted reference to other outcomes from Stapleton *et al* as alleged. No breach of Clause 7.2 was ruled.

Complaint received **7 June 2010**

Case completed **22 July 2010**

DOCTOR v BOEHRINGER INGELHEIM

Journal 'Special Report'

A doctor complained about a four page supplement, 'Preventing Stroke Special Report; "Action or crisis"' which was 'paid for and sponsored by Boehringer Ingelheim' and appeared in the Health Service Journal, 3 June 2010. The complainant noted that supplementary information to the Code stated that 'When a company pays for, or otherwise secures or arranges the publication of promotional material in journals, such material must not resemble independent editorial matter'. The complainant alleged that the supplement did resemble independent editorial matter in that, *inter alia*, the colour scheme, typeface, graphics, spacing, and number of columns were the same as those in the rest of the journal. The complainant alleged a breach of the Code.

The detailed response from Boehringer Ingelheim is give below.

The Panel noted that the article in question was not presented as a supplement. It was presented as a special report and each page included a tab 'Special Report'. The heading to the article 'Preventing Stroke' was followed by the Boehringer Ingelheim logo. Details of the editors and designers were followed by 'This article is paid for and sponsored by Boehringer Ingelheim. Boehringer Ingelheim have had no editorial input into this article'; this statement was repeated at the very end of the article.

In the Panel's view the first matter to be decided was whether or not the article was promotional. The Panel noted that the letter from the Health Service Journal to Boehringer Ingelheim stated that the special reports were not for the purpose of product promotion. It appeared that the article had been initiated by the Health Service Journal. Boehringer Ingelheim had not influenced the content of the article other than to check it for factual accuracy. The article referred to stroke prevention including the use of anticoagulants for people with recognised atrial fibrillation.

The Panel considered that given its content, and Boehringer Ingelheim's role in the arrangements, the article could not be considered promotional. As the article was not promotional it could not be disguised promotion and thus no breach of the Code was ruled.

Upon appeal by the complainant, the Appeal Board considered that the material raised the awareness of the disease area and heightened Boehringer Ingelheim's profile but did not promote its medicines. In that regard it was not promotional and so could not be disguised promotion. The Panel's ruling of no breach of the Code was upheld.

A doctor complained about a four page stroke supplement, 'Preventing Stroke Special Report; "Action or crisis"' that appeared in the Health Service Journal, 3 June 2010.

COMPLAINT

The complainant noted that the supplement was 'paid for and sponsored by Boehringer Ingelheim'. The complainant noted that the supplementary information to Clause 12.1 of the Code stated that 'When a company pays for, or otherwise secures or arranges the publication of promotional material in journals, such material must not resemble independent editorial matter'. The complainant alleged that the supplement did resemble independent editorial matter because the colour scheme, typeface, graphics, spacing, justification, design of the text boxes, font size, call-outs, photograph captions, and number of columns were the same as those in the rest of the journal. The complainant alleged a breach of Clause 12.1.

RESPONSE

Boehringer Ingelheim explained that the article was not in a separate supplement of the Health Service Journal, but a special report in the main journal itself. This was not a promotional piece but an independent, educational editorial by the Health Service Journal. Boehringer Ingelheim provided financial support only towards the publication of this article and had no control of content, other than to check for factual inaccuracies. Sponsorship of this special report was not for the purpose of promotion of any product. The declaration of the sponsorship was mentioned at the outset of the article (page 23) and on page 26 of the Health Service Journal.

Boehringer Ingelheim submitted that the Health Service Journal published these educational reports on stroke prevention in atrial fibrillation because the NHS was very interested in this area via the NHS Heart and Stroke Improvement programme with its recent reports on Commissioning for Stroke: Prevention in Primary Care – The Role of Atrial Fibrillation. As Boehringer Ingelheim had undertaken research in this area, it offered the company an opportunity to support these special reports.

The detailed process for these special reports as agreed with and set out by the Health Service Journal was as follows:

> 'Grants and sponsorship to support Special Reports in the Health Service Journal are used

for:
- Health Service Journal to commission journalists to write the articles and interview chosen individuals
- Health Service Journal to source all illustrations
- Health Service Journal to clear copy with sponsor for factual corrections only
- Health Service Journal to layout and design the special reports.

Boehringer Ingelheim will have no editorial input or control of content, other than for checking for factual inaccuracies. Sponsorship of these Special Reports is not for the purpose of promotion of any product, and full disclosure of sponsorship to support the publication of these Special Reports will be clearly visible.'

Boehringer Ingelheim believed that the material and clarification it had provided clearly complied with the relevant requirements of the Code and did not advocate, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code. Therefore, it denied a breach of Clause 12.1.

PANEL RULING

The Panel noted that the article in question was not presented as a supplement. It was presented as a special report and each page included a tab 'Special Report'. The heading to the article 'Preventing Stroke' was followed by the Boehringer Ingelheim logo. Details of the editors and designers were followed by 'This article is paid for and sponsored by Boehringer Ingelheim. Boehringer Ingelheim have had no editorial input into this article'; this statement was repeated at the very end of the article.

In the Panel's view the first matter to be decided was whether or not the article was promotional. The Panel noted that the letter from the Health Service Journal to Boehringer Ingelheim stated that the special reports were not for the purpose of product promotion. It appeared that the article had been initiated by the Health Service Journal. Boehringer Ingelheim had not influenced the content of the article other than to check it for factual accuracy. The article referred to stroke prevention including the use of anticoagulants for people with recognised atrial fibrillation.

The Panel considered that given the content of the article and Boehringer Ingelheim's role in the arrangements, in that it had no involvement other than providing the sponsorship and checking for factual accuracy, the article in question could not be considered promotional. The article did not promote the prescription, supply, sale or administration of Boehringer Ingelheim's medicines. As the article was not promotional it could not be disguised promotion and thus no breach of Clause 12.1 was ruled.

APPEAL BY THE COMPLAINANT

The complainant noted that in Cases AUTH/2287/12/09 and AUTH/2288/12/09, the Appeal Board ruled a breach of Clause 12.1. The complainant alleged that the material facts were identical in both cases and that therefore the current case must also be ruled in breach of Clause 12.1.

The complainant noted that in both cases a pharmaceutical company paid for an article to appear as a supplement in the Health Service Journal (Boehringer Ingelheim submitted that the article it sponsored was not a supplement, but the front cover of the Health Service Journal described it as a 'Preventing stroke and cutting costs supplement'). In neither case had the pharmaceutical companies any stated input into the article other than to check it for factual accuracy and fund its production. In both cases the article was developed for educational purposes only and did not offer any overt commercial advantage to the pharmaceutical companies in question. Nevertheless both articles were clearly promotional because the pharmaceutical company paid for the publication of an article on a topic for which it had funded research, thereby leading to increased awareness amongst readers about that clinical condition relative to other clinical conditions and therefore increased awareness of treatments which the pharmaceutical company either already marketed or was researching.

The complainant noted that in both cases, the special report appeared as inside pages in the Health Service Journal. Although clear declarations of sponsorship were included at the beginning and end of both articles, readers flicking through the journal, often from back to front, might read one of the inside pages of the supplement without first seeing the declarations of sponsorship. In both cases the editorial style of the supplement was extremely similar if not identical to the standard editorial text of the journal, in that they shared a very similar or identical page layout, typeface, font, font size, colour scheme, number of columns, text boxes, call-outs and so on.

The supplementary information to Clause 12.1 of the Code stated that, 'When a company pays for, or otherwise secures or arranges the publication of promotional material in journals, such material must not resemble independent editorial matter'. The complainant alleged that in both cases, the fact that the text had been sponsored by a pharmaceutical company was disguised to the reader and therefore both cases were in breach of Clause 12.1.

COMMENTS FROM BOEHRINGER INGELHEIM

Boehringer Ingelheim submitted that it had funded the special report after the Health Service Journal had sought financial support (as an unrestricted educational grant) to publish three four page special reports on stroke prevention in atrial fibrillation.

These reports were to focus on the current issues surrounding stroke prevention in atrial fibrillation in terms of cost, commissioning, risk factors and future proofing. Atrial fibrillation was of significant interest to the NHS following the recent reports on Commissioning for Stroke: Prevention in Primary Care – the Role of Atrial Fibrillation.

Boehringer Ingelheim submitted that it had not influenced the educational content of the article other than to check it for factual accuracy.

Boehringer Ingelheim noted that the complainant referred to Cases AUTH/2287/12/09 and AUTH/2288/12/09, however the material facts of that case were very different to the present case. Unlike the previous case, the material now at issue was not a promotional supplement but an independently written educational editorial ('special report') initiated by the Health Service Journal not by Boehringer Ingelheim. In the previous case, the two companies found in breach made a voluntary admission that their supplement should have appeared as a separate piece from the journal.

Boehringer Ingelheim refuted the complainant's allegation that the article was clearly promotional because a pharmaceutical company paid for the publication of an article on a topic for which it had funded research, thereby leading to increased awareness of treatments which the pharmaceutical company either already marketed or was researching. Although the article discussed current treatments (and the benefits thereof), there was no reference to potential future treatments for stroke prevention in atrial fibrillation. Further, the inference that discussion of a disease area would automatically lead to increased awareness of treatments a pharmaceutical company was researching was not substantiable. Equally the article did not promote the prescription, supply, sale, or administration of a medicine and therefore, by definition, was not promotional.

Boehringer Ingelheim noted that the Code did not preclude pharmaceutical companies funding educational, non-promotional articles in journals such as the Health Service Journal. The complainant also alleged that the editorial style of the supplement was extremely similar if not identical to the standard editorial text of the journal and later quoted the supplementary information for Clause 12.1 'When a company pays for, or otherwise secures or arranges the publication of promotional material in journals, such material must not resemble independent editorial matter'. As already stated this was an independently written educational 'special report' initiated by the Health Service Journal; Boehringer Ingelheim's only involvement was to check it for factual accuracy. Therefore, as it was not a 'paid-for' supplement the editorial style of the article was similar to the standard editorial text of the Health Service Journal and appeared as pages 23-26 of the journal. However, it was clearly stated that the article was paid for and sponsored by Boehringer Ingelheim and clearly marked 'Special Report' on pages 23, 25 and 26 of the journal.

Boehringer Ingelheim submitted that it had demonstrated that without doubt the Panel's ruling of no breach of Clause 12.1 was correct, and it strongly refuted the complainant's allegation of disguised promotion.

FINAL COMMENTS FROM THE COMPLAINANT

The complainant alleged that the question of whether the journal first approached the pharmaceutical company, or vice versa did not alter the ultimate fact that Boehringer Ingelheim funded the supplement in question.

Nobody questioned the fact that atrial fibrillation (and rheumatoid arthritis - the topic of the supplement considered in Cases AUTH/2287/12/09 and AUTH/2288/12/09) was of significant interest to the NHS. The respondents in the previous case likewise had not influenced the educational content of their article other than to check it for factual accuracy.

The complainant noted that although Boehringer Ingelheim claimed that the material facts of Cases AUTH/2287/12/09 and AUTH/2288/12/09 were very different from the current case it offered no evidence to demonstrate how this was so. Both cases involved independently written, educational pieces. Whether or not the journal first approached the pharmaceutical company, or the pharmaceutical company first approached the journal, did not affect the nature of the material that appeared in print. Nor did the fact that the respondents in the previous case admitted culpability, whereas Boehringer Ingelheim chose to contest the complaint, affect the material facts of the cases. The rheumatology supplement likewise discussed current treatments (and the benefits thereof) but no potential future treatments were named.

The complainant noted that Boehringer Ingelheim had not stated why his claim that the publication of an article on a topic for which it had funded research would lead to increased awareness amongst readers about that clinical condition relative to other clinical conditions and therefore increased awareness of treatments which the pharmaceutical company either already marketed or was researching, could not be substantiated. There was a wealth of evidence that reading about a disease increased interest in treatments and potential treatments eg the references listed in the notes section in Moynihan and Cassels (2005), 'Selling Sickness: How the Worlds Biggest Pharmaceutical Companies Are Turning Us All Into Patients'.

Nobody doubted that the Code allowed the pharmaceutical industry to fund educational articles in journals such as the Health Service Journal. The crucial point was that such articles must not resemble independent editorial material, and that

the funding must not be disguised from the reader. The complainant alleged that a reader thumbing through the journal and opening the middle page spread (pages 24-25) would have no way of knowing that this was anything other than independent editorial material, and that the article was funded by a pharmaceutical company. The complainant noted that contrary to Boehringer Ingelheim's claim, there was no indication on pages 24 and 25 (the middle pages of the supplement) that the article was paid for and sponsored by the company or that this was anything other than independent editorial content.

The complainant noted that Boehringer Ingelheim did not question his assertion that the editorial style of the supplement was extremely similar, if not identical, to the standard editorial text of the journal.

The complainant noted that Boehringer Ingelheim stated that it paid for the supplement, but that it was not a 'paid-for' supplement. This was patently absurd.

The complainant alleged that he had established that Boehringer Ingelheim paid for the publication of an article in the Health Service Journal that closely resembled independent editorial matter in clear breach of Clause 12.1.

APPEAL BOARD RULING

The Appeal Board noted that Clause 12.1 required that *promotional* material and activities must not be disguised (emphasis added). The Appeal Board considered that it had first to decide whether the material at issue was promotional and in that regard it noted that Clause 1.2 of the Code defined promotion as any activity undertaken by a pharmaceutical company or with its authority which promoted the prescription, supply, sale or administration of its medicines. The Appeal Board disagreed with the complainant's assertion that disease awareness material sponsored by pharmaceutical companies with a commercial or research interest in the therapy area was, ipso facto, promotional.

The Appeal Board noted that the article in question was referred to on the front cover of the Health Service Journal as 'Preventing stroke and cutting costs supplement'. Inside, however, the article was clearly presented as an integral part of the journal (pages 23-26). Pages 23, 25 and 26 included a tab labelled 'Special Report'. The heading to the article 'Preventing Stroke', was followed by the Boehringer Ingelheim logo. Details of the editors and designers were followed by the statement 'This article is paid for and sponsored by Boehringer Ingelheim. Boehringer Ingelheim have had no editorial input into this article'. That statement also appeared at the very end of the article.

The complainant referred to Cases AUTH/2287/12/09 and AUTH/2288/12/09, in which the Appeal Board had previously ruled a breach of Clause 12.1, and alleged that the material facts were identical to the current case. However, the Appeal Board noted that in the previous case the respondents had acknowledged that the 12 page supplement at issue was promotional; it had included on its back cover an advertisement for a medicine which they co-promoted and the companies had had full editorial control. The material now at issue, however, did not include an advertisement for any medicine. Anticoagulation with warfarin or aspirin was referred to in general terms only. Boehringer Ingelheim did not have editorial control other than checking for factual accuracy.

In the Appeal Board's view, the material raised the awareness of the disease area and heightened Boehringer Ingelheim's profile but did not promote Boehringer Ingelheim's specific medicines. In that regard it was not promotional as defined by Clause 1.2. Thus it could not be disguised promotion and so the Appeal Board upheld the Panel's ruling of no breach of Clause 12.1. The appeal was thus unsuccessful.

Complaint received **9 June 2010**

Case completed **8 September 2010**

CASE AUTH/2326/6/10

CONSULTANT HAEMATOLOGIST v BAYER SCHERING PHARMA

Envelope for Kogenate mailing

A consultant haematologist complained about an envelope used by Bayer Schering Pharma to send a Kogenate (recombinant coagulation factor VIII) mailing to patients. The envelope stated 'Good news. A new way to mix your clotting factor'. The letter and leaflet inside were about a new reconstitution kit for Kogenate.

The complainant was concerned that promotional material had been posted to patients with haemophilia A. Some patients who received Kogenate by a home delivery service had received direct mailings from Bayer Schering. In particular, the complainant knew about one patient who felt a gross breach of confidentiality in that he had received a letter through the post with information on the outside that clearly indicated that he was receiving clotting factors and thereby was a haemophiliac. Having discussed this issue with the home delivery company, the complainant realised that Bayer Schering had sent the marketing material in blank (unaddressed) envelopes to the home delivery service company which had then labelled them and posted them to the patients. The complainant was sure that Bayer Schering and the home delivery service realised that was grossly inappropriate. The patient wrote to complain about possible use of his personal details and was concerned that these details were stored at Bayer Schering.

The complainant was concerned that patients' confidentiality had been breached and that Bayer Schering had sought to send promotional information to patients, although the complainant realised that this was probably to inform them of perceived improvements in the product. However, a cynic would suggest that Bayer Schering was also seeking to raise brand awareness. The complainant suggested that Bayer Schering stopped communicating directly with patients about its product. Information about the administration of clotting factors could be given by the medical team looking after the patient.

The detailed response from Bayer Schering Pharma is given below.

The Panel noted that Bayer Schering did not have access to patient details. Patient confidentiality was extremely important and it appeared that this was well understood by Bayer Schering. The mailing in question had been certified for the home delivery service to hand deliver to patients who would be using the new presentation of Kogenate. The home delivery service had mailed the letters following instructions from a Bayer Schering employee that the letters should be sent before the patient received the new presentation. The individual concerned had failed to ensure that the mailing was sent in an (outer) plain envelope.

The Panel noted that the Code permitted pharmaceutical companies to provide information to patients and/or the public about prescription only medicines. Such medicines could not be advertised to the public. The mailing was intended to inform patients already taking Kogenate about changes to its presentation and reconstitution. The Panel queried why it was necessary to refer to such changes as good news on the envelope.

The Panel considered that the claim 'Good news. A new way to mix your clotting factor' was unacceptable for use on an envelope mailed to patients. It put information in the public domain that the addressee was receiving treatment for a medical condition. Patients would have cause to be concerned that a pharmaceutical company had their details. The Panel did not know whether the patients had agreed to receive mailings from Bayer Schering. The Panel considered that high standards had not been maintained and a breach of the Code was ruled as acknowledged by Bayer Schering.

The Panel noted Bayer Schering's submission that the mailing was approved for delivery by the home delivery service, to be delivered by hand with the product pack. The Panel noted that the certificate did not refer to the method of delivery. The Panel noted that such details might appear elsewhere in the job bag. The Panel considered that Bayer Schering had been badly let down by its employee. The Panel decided that the matter was covered adequately by its ruling of a breach of the Code above. On balance the Panel decided to rule no breach of Clause 2 which was reserved to indicate particular censure.

Bayer Schering Pharma made a voluntary admission regarding an envelope (ref UK.PH.HN.KOG 2010.15) containing a mailing to patients about the presentation of Kogenate (recombinant coagulation factor VIII). The envelope stated 'Good news. A new way to mix your clotting factor'. The letter and leaflet inside gave information about a new reconstitution kit for Kogenate. Before deciding whether to treat the matter as a complaint, in accordance with Paragraph 5.4 of the Constitution and Procedure, the Director asked Bayer Schering for additional information.

On receipt of the additional information, it became clear that a consultant haematologist had complained to Bayer Schering about the mailing and copied that complaint to the ABPI. The PMCPA was unable to trace a copy of the letter to the ABPI. A copy was provided by Bayer Schering. Given the circumstances, the Director decided the matter should be considered as a complaint from the consultant. Bayer Schering was so informed.

COMPLAINT

The complainant was concerned that promotional material had been posted to patients with haemophilia A. Some patients, who received Kogenate by a home delivery service, had received direct mailings from Bayer Schering with information about Kogenate. In particular, the complainant had received a specific complaint from a patient who received such promotional material in an envelope with his name and address on the outside and information indicating that he was on clotting factors. Having discussed this issue with the home delivery company, the complainant realised that Bayer Schering had sent the marketing material in blank [unaddressed] envelopes to the delivering company which had then labelled them and posted them to the patient. The complainant was sure that Bayer Schering and the home delivery service realised that was grossly inappropriate. The patient wrote to complain about possible use of his personal details and was concerned that these details were stored at Bayer Schering. Additionally, the patient felt a gross breach of confidentiality in that he had received a letter through the post with information on the outside that clearly indicated that he was receiving clotting factors and thereby was a haemophiliac.

The complainant was concerned that the patients' confidentiality had been breached and that Bayer Schering had sought to send promotional information to patients, although the complainant realised that this was probably to inform them of perceived improvements in the product. However, a cynic would suggest that Bayer Schering was also seeking to raise brand awareness which would be commercially advantageous given that recombinant clotting factors were currently subject to a tendering process.

The complainant wanted assurance from Bayer Schering and the home delivery company that such a breach would not happen again and suggested that Bayer Schering stopped communicating directly with patients about its product. Information about the administration of clotting factors could be given by the medical team looking after the patient.

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

RESPONSE

Bayer Schering stated that 173 patients were sent a user guide in an envelope with the declaration 'Good News – A new way to mix your clotting factor' on the external face as an open mailer. Subsequently two patients telephoned Bayer Schering directly to bring this most regrettable of incidents to its attention. As a result, Bayer Schering made a voluntary admission to the Authority on 10 June 2010. It then became apparent that the company had been overtaken by events when, on 11 June, it received a letter of complaint from a consultant. The letter followed a specific complaint from a patient.

Bayer Schering submitted that the patient should never have received a letter through the post with information on the envelope indicating that he was receiving clotting factor. It was no wonder that he complained and felt a 'gross breach of confidentiality'. Consequently, Bayer Schering replied to the doctor to express its most sincere apologies and to explain how this unfortunate event occurred. Bayer Schering hoped that the doctor would feel able to convey its apologies to his patient.

The letter contained a user guide ('How to prepare Kogenate Bayer for injection') for patients with instructions for reconstituting their clotting factor.

Clearly, information about the administration of clotting factor should be given by the medical team looking after the patient. However, in this case Bayer Schering consulted centres as to whether there should be an additional communication. Two people at the complainant's centre were contacted regarding the use of the home delivery company. The consensus of all of the centres was that this was appropriate and that it should be delivered to patients by hand by the home delivery service when delivering their clotting factor. Consequently, the envelope and user guide were intended to be, and approved for, delivery by the home delivery companies, not by post as an open mailing.

Unfortunately, but for the best of intentions, one of Bayer Schering's employees considered it was important that patients were made aware of the relevant information prior to delivery of their clotting factor so that they were prepared for the change. The individual concerned believed that patients should be informed of the change to their treatment as soon as possible. As a result the delivery company was instructed to send the mailer before delivering the clotting factor to patients. Unhappily, as the company was acutely aware, the individual did not emphasize the need to enclose the mailing in a [outer] plain envelope.

As part of the tendering process there was user testing of the reconstitution devices provided by the different companies. It was a condition of the contract that a specific reconstitution device was used. The letter was sent by the delivery service to patients because Bayer Schering had been requested to change the reconstitution device for its clotting factor. It was not an attempt to send

promotional information to patients or to communicate directly with them.

It could not be over-emphasised that Bayer Schering did not store, or wish to store, personal details of patients. Patient details were only held by the delivery companies which were engaged by the centres and instructed by them as to which patients should receive clotting factor. The delivery companies were not third party service providers to Bayer Schering.

The letter was sent after contracts had been awarded and only to those patients whom the centres had decided would receive Kogenate.

In summary, the envelope and enclosed letter and user guide were intended, and as such approved, to be delivered by the home delivery service and not sent through the post as an open mailing. In other words it was certified for delivery by hand with the product pack.

Regrettably this unacceptable event was a consequence of an individual not following the instructions for how the mailing was to be used. Having instructed the delivery services to send the mailing prior to delivery of the product, this was compounded by the failure to ensure that all of the delivery companies understood that it was inappropriate to send a letter through the post with information on the outside indicating that patients were receiving clotting factor.

Bayer Schering hoped that it was accepted that this regrettable incident was the consequence of an unwitting failure on the part of an individual whose only intention was to do what they thought was best for the patients, that was to inform them of the change to reconstitution of their clotting factor as soon as possible.

A number of actions were taken when this most unfortunate of events came to light. All the delivery companies were contacted in order to draw the matter to their attention and request that no further open mailings should be sent. There had been an investigation as to how this happened together with a full and frank discussion with the individual concerned. Bayer Schering's medical governance function subsequently sent an internal communication requiring senior managers to reinforce awareness within their teams that the delivery of items should be in accordance with the instructions provided in the certified job bag.

This incident was a failure to maintain high standards, hence Bayer Schering's voluntary admission. Having conveyed its most sincere apologies to the complainant, Bayer Schering now extended them to the Authority.

PANEL RULING

The Panel noted that Bayer Schering did not have access to patient details. Patient confidentiality was extremely important and it appeared that this was well understood by Bayer Schering. The mailing in question had been certified under Clause 14 for the home delivery service to hand deliver to patients who would be using the new presentation of Kogenate. The home delivery service had mailed the letters following instructions from a Bayer Schering employee that the letters should be sent before the patient received the new presentation. The individual concerned had failed to ensure that the mailing was sent in an [outer] plain envelope.

The Panel noted that Clause 22 permitted pharmaceutical companies to provide information to patients and/or the public about prescription only medicines. Such medicines could not be advertised to the public. The mailing was intended to inform patients already taking the medicine about changes to the presentation and reconstitution of Kogenate. The patient would already be aware of the product. However the Panel queried why it was necessary to refer to the changes as good news on the envelope.

The Panel considered that the claim 'Good news. A new way to mix your clotting factor' was unacceptable for use on an envelope mailed to patients. It put information in the public domain that the addressee was receiving treatment for a medical condition. It would also cause patients to be concerned that a pharmaceutical company had their details. The Panel did not know whether the patients had agreed to receive mailings from Bayer Schering. The Panel considered that high standards had not been maintained and a breach of Clause 9.1 was ruled as acknowledged by Bayer Schering.

The Panel noted Bayer Schering's submission that the mailing was approved to be delivered by the home delivery service. It was certified for delivery by hand with the product pack. The Panel noted that the certificate recorded the intended use/purpose/distribution as 'To inform patients about the new reconstitution kit'. There was no reference to the method of delivery. The Panel noted that such details might appear elsewhere in the job bag. The Panel considered that Bayer Schering had been badly let down by its employee. The Panel decided that the matter was covered adequately by its ruling of a breach of Clause 9.1 above. On balance the Panel decided to rule no breach of Clause 2 which was reserved to indicate particular censure.

Complaint received **22 June 2010**

Case completed **3 August 2010**

TRUST CLINICAL DIRECTOR v PFIZER

Conduct of representative

A clinical director of a mental health foundation trust complained about the conduct of a Pfizer representative in that nursing staff had described the representative as 'quite intimidating' in trying to access them. He had attended clinical areas and asked the receptionists if he could meet nursing colleagues then, without an appointment. Receptionists and nursing staff reported how he had then waited in that area, where patients and relatives were moving from the waiting room to clinics and then accosted nursing staff who moved through that area.

On other occasions when the representative had no appointment and being told that staff were not able to meet him, staff had described how he sat in that area and worked on his laptop and then accosted nursing staff when they walked past.

Nursing staff also described feeling enormous pressure when attending to urgent visits recently and, on going out into the car park when on the telephone, described how the representative 'leapt out of his car, opened his boot and dashed over to talk to me (when I was clearly on the phone)'. Staff considered that this was inappropriate pressure and conduct.

The detailed response from Pfizer is given below.

The Panel noted that the complainant alleged that nursing staff had described the representative as 'quite intimidating' when trying to access them and had asked receptionists and other staff about meeting nursing colleagues without appointments. It appeared from Pfizer's submission that on the day in question the representative did not have an appointment. The representative arrived at 8.50am and was let into the unit by a nurse. The representative had waited for the receptionist to arrive who then attended to him. The representative failed in his attempt to see nurse 'B' and to elicit his interest in attending a meeting. The representative then asked to see nurse 'A' but she was busy. The representative stated that he had not seen any patients. Twelve minutes after his arrival the representative returned to his car in the car park and did some administration. Nurse 'A' appeared in the car park as the representative was putting his computer in the boot. The complainant alleged that the representative had 'dashed over to talk to the nurse' whereas the representative stated that he did not leave the back of his car, he did not rush over to the nurse and no words were exchanged.

The Panel did not consider that the complaint was limited to the events of one day as presumed by the representative. However the Panel noted the representative's submission that he had never had cause to think that his visits to the unit were inconvenient or that his presence was interfering or causing any offence.

When provided with Pfizer's response, the complainant stated that he had no further comments to add. The Panel noted that it was clear that the staff had been upset and this was most unfortunate. The Code required that representatives' calls should not cause inconvenience to those upon whom they call. Representatives should be mindful of the impression created by their conduct particularly when they did not have appointments.

Nonetheless, given the information before it, the Panel decided it was not possible to determine precisely what had occurred and thus ruled no breach of the Code.

A clinical director of a mental health foundation trust complained about the conduct of a Pfizer Limited representative.

COMPLAINT

The complainant stated that the representative had operated in a way that was not congruent with the Code. Nursing staff had described him as 'quite intimidating' in trying to access them. He had attended clinical areas (such as an outpatient clinic within a day hospital) and asked the receptionists if he could meet nursing colleagues then, without an appointment. Receptionists and nursing staff reported how he had then waited in that area, where patients and relatives were moving from waiting room to memory clinic to outpatient clinic and then accosted nursing staff who moved through that area.

On other occasions when the representative had no appointment and being told that staff were not able to meet him, staff had described how he sat in that area and worked on his laptop and then accosted nursing staff when they walked past.

Nursing staff also described feeling enormous pressure when attending to urgent visits recently and, on going out into the car park when on the telephone, described how he 'leapt out of his car, opened his boot and dashed over to talk to me (when I was clearly on the phone)'. Staff considered that this was inappropriate pressure and an inappropriate way for a representative to conduct himself.

When writing to Pfizer, the Authority asked it to respond in relation to Clauses 9.1, 15.2, 15.4 and 15.9 of the Code.

RESPONSE

Pfizer provided the representative's own written account of his visit to the unit on 23 June.

Pfizer stated that in summary the representative arrived at the unit at 8.50am on 23 June in order to ensure he would arrive prior to any patient clinics. This was the representative's third visit to the unit in 2010 – the first was to invite nurse 'A' to speak at a Pfizer dementia educational meeting and the second was to deliver patient information leaflets and information about a patient carer support programme. The purpose of the visit on 23 June was to invite nurse 'B' to the 12th National Memory Conference.

As nurse 'B' was unavailable, the representative asked to speak to nurse 'A' to see if she would be interested in attending the conference instead. Nurse 'A', however, was unavailable and so at approximately 9.02am the representative left the unit. Although the representative later saw nurse 'A' after leaving the unit, no words were exchanged as the representative knew she was on the telephone.

From the representative's account he had 'visited the unit 3 times this year' (including the visit on the 23 June). In line with the supplementary information to Clause 15.4 that the number of calls made on a doctor or other prescriber by a representative each year should not normally exceed three on average, Pfizer did not believe that it was in breach of Clause 15.4.

Pfizer believed that the representative conducted himself in a professional and ethical manner and that high standards were met. The representative had passed his ABPI Medical Representatives Examination with distinction and had no history of complaints regarding his professional conduct. Highlighting this, the representative stated that at no point during this or any previous visit was he given the indication that his presence was 'interfering', 'causing any offence' or 'inconvenience'. Pfizer therefore also believed that no breach of Clause 15.2 occurred.

Pfizer provided copies of a sales team brief. This briefing material for the 12th National Memory Clinic Conference invitations process set out clear instructions for representatives with regard to identifying appropriate health professionals to invite to the meeting, distribution of invitations, registration and follow-up with delegates to confirm attendance. Pfizer did not believe the material to be in breach of Clause 15.9.

In summary, Pfizer believed it had consistently maintained high standards, was not in breach of Clauses 9.1, 15.2, 15.4 or 15.9 and that the representative acted professionally, in an ethical manner and complied with the requirements of the Code.

In his account, the representative stated that as there were no specific dates he presumed that the alleged complaint occurred on 23 June. The only other occasions that he had been in the unit in 2010 were in February. In the year to date he had not contacted or met any member of the nursing teams in the unit more than three times.

The representative stated that he arrived at the unit at 8.50am with the intention of trying to catch nurse 'B' to ask if he would be able to attend the 12th annual memory conference. The representative arrived before 9.00am to make sure that he would not arrive as clinics were taking place. When he arrived there was no receptionist at the main desk so he was let into the unit by nurse 'C' who was passing. He asked nurse 'C' if there were any clinics underway, she confirmed that there were none. The representative explained to her that he had come to offer nurse 'B' a place at the memory conference, and asked if it was okay to wait. The representative noted that at no time whilst in the unit did he see or come into contact with any patients, none had arrived. The representative quickly had a word with nurse 'C' and sat alone in the waiting area. When the receptionist arrived he asked if it would be possible to catch nurse 'B' for a couple of minutes. The receptionist said that he was in the building but she didn't know where. The representative asked the receptionist if she would be kind enough to telephone to find out where he was, and if he was free. After a couple of minutes trying she was unable to locate him. The representative then proceeded to write the meeting dates on a business card and asked if she would ask nurse 'B' to let him know if he was interested. The representative was about to leave when he came through a door next to him. The representative asked if he had a minute to look at the invite and he promptly said no and walked past without stopping. The representative then asked the receptionist if she could see if nurse 'A' had a couple of minutes to ask if she would possibly be interested if nurse 'B' could not attend. The receptionist telephoned, and said that nurse 'A' was busy. The representative thanked the receptionist and left the unit. The time was approximately 9.02am.

After visiting the unit the representative sat in his car to put in a couple of calls and make a few telephone calls (effectively the car was his office). As he put his computer into the back of his car nurse 'A' walked out of the unit on the telephone, and he acknowledged her by raising his hand. The representative made clear that he did not leave the back of his car, nor did he rush over to her and no words were exchanged, as he knew she was on the telephone. He was just trying to be polite.

In the past the representative had never been informed that he could not visit the unit, and had never been asked to leave the unit, nor was it suggested that he was causing any inconvenience.

He had visited the unit three times this year including the visit above. On one occasion it was by appointment to ask nurse 'A' if she would speak for Pfizer for an educational meeting on early dementia. The only other occasion was in February to drop off patient information leaflets and information about the patient carer support programme.

Up until receiving the complaint the representative had never had any indication from anyone in the unit that his presence was interfering or causing any offence. If this was the case he would of course have left immediately. He was truly shocked and distressed by these allegations as he thought he had always, over several years, had a good working relationship with this unit. He was fully aware of the rules regarding conduct outlined in the Code and had always strived to fully uphold these.

FURTHER COMMENTS FROM THE COMPLAINANT

Pfizer's response was sent to the complainant who stated he had no further comments to add.

PANEL RULING

The Panel noted that the complaint was from a clinical director on behalf of nursing and reception staff. The details submitted by each party differed and so it was difficult to determine where the truth lay. A judgement had to be made on the available evidence bearing in mind the extreme dissatisfaction usually necessary on the part of an individual before he or she was moved to submit a complaint. The Panel noted that it was for the complainant to establish his case on the balance of probabilities.

The Panel noted that the complainant alleged that nursing staff had described the representative as 'quite intimidating' when trying to access them and had asked receptionists and other staff about meeting nursing colleagues without appointments. It appeared from Pfizer's submission that on 23 June the representative did not have an appointment with any of the staff at the unit in question. The representative arrived at 8.50am and was let into the unit by nurse 'C'. The representative had waited for the receptionist to arrive who then attended to him. The representative failed in his attempt to see nurse 'B' and to elicit his interest in attending a meeting. The representative then asked to see nurse 'A' but she was busy. The representative stated that he had not seen any patients. Twelve minutes after his arrival the representative returned to his car in the car park and did some administration. Nurse 'A' had appeared in the car park as the representative was putting his computer in the boot. The complainant alleged that the representative had 'dashed over to talk to [the nurse]' whereas the representative stated that he did not leave the back of his car, he did not rush over to the nurse and no words were exchanged.

The Panel did not consider that the complaint was limited to the events of 23 June as presumed by the representative. However the Panel noted the representative's submission that in the past he had never had cause to think that his visits to the unit were inconvenient; no-one at the unit in question had previously indicated that his presence was interfering or causing any offence.

When provided with Pfizer's response for comment the complainant stated that he had no further comments on the matter. The Panel noted that it was clear that the staff had been upset and this was most unfortunate. The Code required that representatives' calls should not cause inconvenience to those upon whom they call. Representatives should be mindful of the impression created by their conduct particularly when they did not have appointments.

Nonetheless, given the information before it, the Panel decided it was not possible to determine precisely what had occurred and thus ruled no breach of Clauses 9.1, 15.2, 15.4 and 15.9 of the Code.

Complaint received **1 July 2010**

Case completed **23 August 2010**

ASTELLAS PHARMA EUROPE v GENUS

Eczmol journal advertisement

Astellas Pharma Europe complained about a journal advertisement for Eczmol (chlorhexidine gluconate cream) issued by Genus. Eczmol was an antimicrobial emollient which could also be used as a soap substitute in the management of dry and pruritic skin conditions including eczema and dermatitis. Astellas supplied Locoid (hydrocortisone-17-butyrate) a topical corticosteroid available in a number of presentations, including a cream, for the treatment of steroid responsive conditions such as eczema, dermatitis and psoriasis.

Astellas stated that a series of three Locoid advertisements were created in early 2009. Printed materials were distributed to customers in May 2009 and the advertisements were first published in October 2009 (BMJ International, week commencing 5 October). The advertisements were also subsequently published in the New England Journal of Medicine.

Astellas first became aware of the Eczmol advertisement on 17 May 2010; it knew of only one version of the advertisement which as far as it was aware, first appeared in the BMJ on 8 May 2010, one year after the first release of the Locoid advertisements.

Astellas alleged that the overall copy, tagline and general layout of the Eczmol advertisement was similar to that of the Locoid advertisements. In particular:

- **the image of a gentle animal with a shadow of a strong animal. This was highly conceptually similar to the three Locoid advertisements which respectively contained images of strong animals formed from images of gentle animals, soft toys or gentle insects. This visually emphasised the message 'gentle/strong' theme of each of the advertisements.**
- **the tagline 'Gentle yet strong', which was a direct inversion of 'Strong but gentle' used by Astellas. This directly linked into the similar animal imagery used in all of the advertisements.**
- **the two tonal strong purple background, which reflected the strong aubergine, green and burnt orange two tonal backgrounds in the Locoid advertisements.**
- **the various elements in the Eczmol advertisement had a very similar overall positioning to the various elements in the Locoid advertisements.**

Astellas alleged that as a whole, the Eczmol advertisement could only have been copied from the Locoid advertisements.

Astellas stated that there could be no doubt that the same consumers would be exposed to both the advertisements. Given the strong visual and conceptual similarities between the advertisements and that Eczmol and Locoid were used to treat the same condition, there was a strong likelihood that those consumers would be misled or confused into believing that the products were effectively interchangeable.

There was a risk that the target audience would wrongly associate the products and consequently might treat their patient with the incorrect product. Astellas considered that there were significant public health consequences of such confusion.

The detailed response from Genus is given below.

The Panel noted that the Code stated that promotional material must not imitate the devices, copy, slogans or general layout adopted by other companies in a way that was likely to mislead or confuse.

The Panel noted that in the advertisements for Locoid and the advertisement for Eczmol there was a common theme in that animals were in some way portrayed as their opposites ie in the Eczmol advertisement a real lamb appeared to cast the shadow of an ox, hence the headline 'Gentle yet Strong' and in the Locoid advertisements images of strong animals were composed of multiple pictures of soft animals, hence the claim 'Strong but gentle topical treatment' which appeared beneath the image of the animal. The Eczmol advertisement stated that Eczmol was a cream with antimicrobial power to deal with *Staph aureus* associated with ectopic eczema. Details of its active ingredient and use as an antimicrobial emollient and soap substitute were included in the copy immediately below the brand name which was very clearly given in bold type. The Locoid advertisements had less copy; it was made it clear that the product contained hydrocortisone and it was stated that its safety profile was that of a mild corticosteroid. The Panel considered that although the advertisements shared a common theme, ie the use of animal opposites in relation to the words 'strong' and 'gentle', the execution of the concept was different.

The Panel noted that Locoid and Eczmol might both, on occasion, be used by the same patient. The two products, however, belonged to different therapeutic classes of medicine. In the Panel's view

the advertisements were unlikely to mislead readers such that they might believe that Locoid, a topical steroid, and Eczmol, an antimicrobial emollient, were interchangeable as alleged. Astellas had not produced any evidence to show that health professionals had been misled in this way.

The Panel noted that although there were some similarities between the advertisements it did not consider that the Eczmol advertisement imitated the Locoid advertisements in a way that was likely to mislead or confuse readers. No breach of the Code was ruled.

Astellas Pharma Europe Ltd complained about a journal advertisement (ref ECZ0110659) for Eczmol (chlorhexidine gluconate cream) issued by Genus Pharmaceuticals Ltd. Eczmol was an antimicrobial emollient which could also be used as a soap substitute in the management of dry and pruritic skin conditions including eczema and dermatitis. Astellas supplied Locoid (hydrocortisone-17-butyrate) a topical corticosteroid available in a number of presentations, including a cream, for the treatment of steroid responsive conditions such as eczema, dermatitis and psoriasis. Inter-company dialogue had failed to resolve the matter.

COMPLAINT

Astellas stated that a series of three Locoid advertisements were created in early 2009. Printed materials were distributed to customers in May 2009. The advertisements appeared on a regular basis in the BMJ International starting with the edition published in the week commencing 5 October. The advertisements also appeared regularly in the New England Journal of Medicine starting with the edition published in the week commencing 19 October. The publication schedule was currently planned to run until 2011.

Astellas considered that the Locoid advertisements were visually and conceptually unique and that there was nothing else like them on the general market, pharmaceutical or otherwise.

Astellas first became aware of the Eczmol advertisement on 17 May 2010; it knew of only one version of the advertisement. As far as Astellas was aware, the Eczmol advertisement first appeared in the BMJ on 17 April 2010, one year after the first release of the Locoid advertisements, and thereafter on a fortnightly publication schedule. Imagery from the advertisement also appeared on the website www.Eczmol.co.uk extracts of which were provided.

Astellas alleged there were many aspects of similarity between the Eczmol advertisement and the Locoid advertisements, including the overall copy, tagline and general layout. In particular:

- the Eczmol advertisement featured the image of a lamb (a gentle animal) with a shadow of a bull (a strong animal). This was highly conceptually similar to three Locoid advertisements which respectively contained images of the following strong animals, a lion formed from images of kittens (gentle animals), a bear formed from images of teddy bears (soft toys) and a rhinoceros formed from images of butterflies (gentle insects). This visually emphasised the message 'gentle/strong' theme of each of the advertisements, discussed further below.

- the Eczmol advertisement used the tagline 'Gentle yet strong', which was a direct inversion of 'Strong but gentle' used by Astellas in all three Locoid advertisements. This directly linked into the similar animal imagery used in all of the advertisements.

- the Eczmol advertisement had a two tonal strong purple background, which reflected the strong aubergine, green and burnt orange two tonal backgrounds in the Locoid advertisements.

- the various elements in the Eczmol advertisement had a very similar overall positioning to the various elements in the Locoid advertisements including the animal in the top two thirds of the advertisement and the placement of the product descriptor (ie 'Eczmol contains…the skin' and 'Strong but gentle…corticosteroid').

Astellas alleged that as a whole, the Eczmol advertisement could only have been copied from the Locoid advertisements.

Given that Genus knew about the Locoid advertisements (when the Eczmol product manager attended a ceremony at which Astellas received an award for them in January 2010) and that the Eczmol advertisement was first published after that date, Astellas submitted that it was an imitation of the Locoid advertisements that was likely to mislead or confuse.

Both Eczmol, an antiseptic emollient and Locoid, a topical corticosteroid, were used to treat atopic eczema.

In inter-company dialogue Genus had suggested that the Locoid advertisements and the Locoid product were targeted to an international specialist/secondary audience. Genus sought to distinguish the target audience of Eczmol, which was considered to be UK GPs. Astellas had categorically informed Genus on several occasions that this was not the case. It was not possible to distinguish the target audience of the products in this way; Locoid was targeted at physicians of all levels, including those in the UK, particularly GPs. It was conceivable that both Locoid and Eczmol would be used to treat the same condition in one patient. Therefore, Genus' comment that the products were 'used in different contexts' was incorrect.

Given that the Locoid advertisements and the Eczmol advertisement were both targeted towards the same audience (practitioners at all levels, including GPs) and had the same market (the UK) there could be no doubt that the same consumers would be exposed to the advertisements. Given the strong visual and conceptual similarities between the advertisements and that the products were used to treat the same condition, there was a strong likelihood that those consumers would be misled or confused into believing that the products were effectively interchangeable.

Astellas considered that the arguments advanced by Genus, which sought to distinguish the advertisements, were semantic at best; GPs reviewing the advertisements would not stop to analyse the conceptual differences between 'strong but gentle' and 'gentle but strong'. They would also not break down the subtle differences in the 'characteristics' of the animals posited by Genus. Rather, in the context of the conceptually and visually similar advertisements that related to products that were used to treat the same condition, there was a risk that the target audience would wrongly associate the products and consequently might treat their patient with the incorrect product. Astellas considered that there were significant public health consequences of such confusion.

For the reasons above, Astellas alleged that the Eczmol advertisement was an imitation of the copy, taglines, and general layout of the Locoid advertisement in a way that was likely to mislead or confuse in breach of Clause 9.4 of the Code.

RESPONSE

Genus stated that an advertising agency [not the one employed by Astellas] was asked to develop an original advertising concept for Eczmol in September 2009. The Brand Concept Diagram was completed by 29 September and the 'Baary' (name of the lamb in the advertisement) concept was initially presented to Genus on 12 October. Revised concepts were then emailed to Genus on 21 October ie the day before the Locoid advertisement was first published in the UK in the New England Journal of Medicine. Genus and its agency thus had not imitated the devices, copy, slogan or general layout adopted by Astellas in a way that was likely to mislead or confuse.

For reasons not applicable to this case there was a subsequent delay in the launch of Eczmol and hence a delay in the advertisement being published.

The Eczmol Baary concept was a very clear conceptual image that simply depicted a 'real live' lamb that had the shadow of an ox. This image was specifically designed to represent the simplicity of the product and was very basic in design. It also represented the history of the product development from real life experience. This was conceptually very different from the complex design of the Locoid advertisements. The Locoid advertisement used many small, soft furry animals to make up one large fierce, wild animal.

The animals (or toys) used in the Locoid advertisements could not be confused with 'real life' animals and therefore it seemed extraordinary that they could be considered a source of confusion between products or indeed any form of imitation.

The Eczmol advertisement simply stated 'Gentle yet Strong', the Locoid advertisement stated 'Strong but gentle topical treatment'. These statements were not directly related and therefore 'imitation' was not applicable. If the basis of the argument was around the two words then the entire industry must be held to account with statements such as 'fast and effective' or 'dual action'. These words were entirely suitable and reasonable as descriptors of unique selling points of both products and neither company should reasonably be able to claim a monopoly on their use. The fact that they were not even used in the same order, and the rhythm, tone and strapline lengths were so different added to the vexatious nature of this complaint.

The Eczmol advertisement incorporated two colour tones which were unblended and used to infer a horizon. If the horizon did not exist then the lamb could not appear to be standing on the ground therefore the shadow concept would not work. The Locoid advertisements had blended and shaded tones that were also far more vivid in nature. Again Genus contended that the two were effectively different.

There were two places of similar positioning between the advertisements and these were standard in most pharmaceutical advertisements which were in portrait orientation. The prescribing information was at the bottom and the logo was at the bottom right. The actual concept pieces of the advertisements differed as the placement of the animals and the tag lines were in very different positions. Again Genus found it difficult to see how this could be considered imitation.

Genus submitted that the initial concepts of the design and formats were completed before the publication of the Locoid advertisement and in reality the concepts were very different from one another.

Genus did not believe that there was any basis in the complaint that the Eczmol advertisement was likely to mislead or confuse the intended audience, or indeed anyone viewing these advertisements. The advertisements themselves were conceptually different and visually the colour schemes were not similar; health professionals were unlikely to confuse them.

Genus further argued that the main active ingredients within the two products had been prescribed in the UK for many years. Hydrocortisone was known to be a steroid by UK physicians and Locoid was positioned as a potent

steroid with the safety profile of a mild corticosteroid. The indication for Locoid was 'conditions responsive to topical steroids'. Locoid would therefore be prescribed and promoted against all of these conditions. In MIMS (July 2010) Locoid was correctly placed in the inflammatory skin conditions section. Chlorhexidine was known to be an antimicrobial or antiseptic. Eczmol, due to its 8% emollient base was indicated for dry and pruritic skin conditions and was within the eczema, pruritic, dry skin conditions section of MIMS. Eczmol was specifically promoted to combat *Staph aureus* in eczema.

Genus submitted that there was no reasonable likelihood of confusion between these two products as they were specifically promoted to improve differing conditions and underlying factors. Furthermore the trade names of the products were so different as to make confusion even more unlikely. As the audience was qualified health professionals the likelihood of any confusion decreased yet further and therefore Genus could not agree with the suggestion that there were any consequences for public health.

In addition to the above and despite ongoing promotion of Eczmol to UK health professional audiences, Genus had yet to hear any mention of Locoid from its customers. Therefore this alleged perceived risk did not appear to be seen in real life.

Genus made no comment regarding its belief that Locoid in this promotional exercise was directed to non-UK audiences as it appreciated that UK physicians might on occasions be exposed to non-UK advertisements, but it firmly believed that the above arguments were a robust rebuttal of the accusation.

For all the rationales included above, Genus was surprised by the ongoing nature of this complaint because the two advertisements were developed independently, the concepts were different in design, they were not visually similar and the products were for different indications.

Genus therefore denied a breach of Clause 9.4.

PANEL RULING

The Panel noted that Clause 9.4 stated that promotional material must not imitate the devices, copy, slogans or general layout adopted by other companies in a way that was likely to mislead or confuse.

The Panel noted that in the advertisements for Locoid and the advertisement for Eczmol there was a common theme in that animals were in some way portrayed as their opposites ie in the Eczmol advertisement a real lamb appeared to cast the shadow of an ox, hence the headline 'Gentle yet Strong' and in the Locoid advertisements images of strong animals were composed of multiple pictures of soft animals, hence the claim 'Strong but gentle topical treatment' which appeared beneath the image of the animal. The Eczmol advertisement stated that Eczmol was a cream with antimicrobial power to deal with *Staph aureus* associated with ectopic eczema. Details of its active ingredient and use as an antimicrobial emollient and soap substitute were included in the copy immediately below the brand name which was very clearly given in bold type. The Locoid advertisements had less copy than the Eczmol advertisements. The Locoid advertisements made it clear that the product contained hydrocortisone and referred to its safety profile as that of a mild corticosteroid. The Panel considered that although the advertisements shared a common theme, ie the use of animal opposites in relation to the words 'strong' and 'gentle', the execution of the concept was different.

The Panel noted that Locoid and Eczmol might both, on occasion, be used by the same patient. The two products, however, belonged to different therapeutic classes of medicine. In the Panel's view the advertisements were unlikely to mislead readers such that they might believe that Locoid, a topical steroid, and Eczmol, an antimicrobial emollient, were interchangeable as alleged. Astellas had not produced any evidence to show that health professionals had been misled in this way.

The Panel noted that although there were some similarities between the advertisements it did not consider that the Eczmol advertisement imitated the Locoid advertisements in a way that was likely to mislead or confuse readers. No breach of Clause 9.4 was ruled.

Complaint received **2 July 2010**

Case completed **9 August 2010**

CASE AUTH/2330/7/10

ANONYMOUS v GRÜNENTHAL

Promotion of unlicensed indication in poster presentation

An anonymous and uncontactable complainant submitted an item headed 'Localised Neuropathic Pain' which referred to Versatis (lidocaine plaster) a product supplied by Grünenthal. At the foot of the one page document, in very small type, were the words 'Sponsored by an unrestricted grant by Grünenthal UK Ltd'.

Versatis was indicated for the symptomatic relief of neuropathic pain associated with previous herpes zoster infection (post-herpetic neuralgia, PHN).

The complainant had highlighted: 'Conclusion, Versatis has an "off-label" use for the symptomatic relief of localised neuropathic pain, and could provide a substantial saving to the local health-economy'. The Director interpreted this as an allegation that the document promoted Versatis for an unlicensed indication.

In its detailed response, given below, Grünenthal explained that the item provided by the complainant had the same copy as a poster submitted to the poster session of a meeting of the British Pain Society (BPS) and the accompanying handout.

The Panel noted that Grünenthal had paid for the printing of the poster and had helped with its submission to the BPS; the company stated that it had not had editorial control of the poster. A consultant pharmacist appeared to have led on the development of the poster. The Panel did not know if the consultant pharmacist had been paid by Grünenthal in relation to the poster or had been otherwise retained by the company. A Grünenthal employee had provided information for the poster and was named as the second author although her position with Grünenthal was not declared. The Panel considered it was unacceptable of Grünenthal not to make it clear in its response that one of its employees was named as an author. The Panel considered that given that one of the named authors was a Grünenthal employee, the company could not dissociate itself from the content of the poster. It was difficult to see how in these circumstances Grünenthal could submit it had no editorial control.

The Panel noted that the material provided by the complainant was not the same size as either the poster or the handout; in that regard the material submitted could be a reproduction of either. The complainant had highlighted the phrase 'Versatis has an "off-label" use for the symptomatic relief of localised neuropathic pain, and could provide a substantial saving to the local health-economy'. In the Panel's view this was clearly a complaint about that sentence which appeared on the poster and the handout. The Panel considered the two items separately.

The Panel then considered whether the poster formed part of the legitimate exchange of medical and scientific information during the development of a medicine as submitted by Grünenthal. The certificate showed that the company had purported to approve it as promotional material. The Panel noted that the poster reported the outcome of a retrospective analysis of published literature (after 2000) on the treatment options for localised neuropathic pain. Electronic prescribing data from a primary care trust with a patient population of 500,000 was used as a basis of assumptions for the algorithm. The poster stated that recent literature showed that '…only 1% of PHN patients are prescribed Versatis patches first-line for PHN pain' and approximately 5% of patients trialled on gabapentin and pregabalin tried Versatis as second line. From this the authors predicted that 143 patients from a population of 500,000 would benefit from Versatis in PHN.

The results section referred to prescribing Versatis for the symptomatic relief of localised neuropathic pain and quantified the yearly savings that could be made by using Versatis compared with the cost of gabapentin at 3.6g/day or pregabalin.

The discussion section referred to the challenges of treating neuropathic pain in part due to its multiple aetiologies, symptoms and underlying mechanisms. The review highlighted the various pharmacological options for symptomatic treatment of localised neuropathic pain. It was stated that Versatis was an equitable option for pain management competing with gabapentin and pregabalin as a cost-effective choice and provided a saving to the local health-economy.

The Panel did not consider that the subject of the poster, the cost implications of prescribing Versatis in an unlicensed indication, contributed to the legitimate exchange of medical and scientific information during the development of a medicine as meant by supplementary information to the Code. The Panel queried whether the information presented contributed to the development of the medicine as it could be argued that the information was neither scientific nor medical. In the Panel's view discussion of unlicensed indications was more likely to be seen as promotional when products were already available on the market albeit for different indications. Overall the Panel did not consider that the poster could claim the benefit of the exemption. In the Panel's view the poster

advocated using Versatis for localised neuropathic pain instead of gabapentin or pregabalin solely on the basis of cost. The poster also included a section 'Potential Costing Savings (for PHN)'. The Panel noted that treatment of PHN, a specific type of neuropathic pain, was within the Versatis marketing authorization.

The Panel noted that the abstract for the poster differed from the poster in a number of ways. For example, the abstract clearly stated that a named person was a health economy liaison manager, Grünenthal. Unlike the poster the abstract did not mention the 'off-label' use of Versatis. It was stated in the abstract that the pharmacist and his colleague (the second author named in the abstract and named as third author on the poster/handout) 'received and [sic] educational grant from Grünenthal Ltd for the development of the algorithm'. The poster included a copy of the algorithm, supporting statements, costing estimates and potential cost savings for PHN which were not included in the abstract. The abstract had four references 1-4. The poster cited these four references, listed 1-4, plus another set of references separately numbered 1-29.

The Panel considered that given Grünenthal's role in the production of the poster and its content it was promotional material and thus covered by the Code. The claim at issue promoted Versatis for an unlicensed indication and thus the Panel ruled a breach of the Code. The Panel considered that high standards had not been maintained and ruled a breach of the Code.

The Panel noted that Clause 2 was a sign of particular censure and reserved for such use. The Panel noted its comments above. The Panel was especially concerned that the company had certified the promotional item which referred to an unlicensed indication knowing that it would appear as part of a peer-reviewed poster presentation at a scientific conference. The Panel considered that delegates would be likely to view the material and the statement at issue differently if they knew it was promotional material. The Panel considered that overall the company's activities reduced confidence in the pharmaceutical industry and thus ruled a breach of Clause 2.

The Panel noted Grünenthal's submission that the handout had not been used. In the circumstances the Panel ruled no breach in that regard.

An anonymous and uncontactable complainant submitted an item headed 'Localised Neuropathic Pain' which referred to Versatis (lidocaine plaster) a product supplied by Grünenthal Ltd. At the foot of the one page document, in very small type, were the words 'Sponsored by an unrestricted grant by Grünenthal UK Ltd'.

Versatis was indicated for the symptomatic relief of neuropathic pain associated with previous herpes zoster infection (post-herpetic neuralgia, PHN).

COMPLAINT

The complainant had highlighted: 'Conclusion, Versatis has an "off-label" use for the symptomatic relief of localised neuropathic pain, and could provide a substantial saving to the local health-economy'.

The Director interpreted this as an allegation that the document promoted Versatis for an unlicensed indication. Grünenthal was asked to respond in relation to Clauses 2, 3.2 and 9.1 of the Code.

RESPONSE

Grünenthal submitted that the item was never approved for promotional use. It was certified as a poster handout.

A consultant pharmacist and his colleague had an informal discussion with the Grünenthal market access director about his local health economic data and getting it published as part of the legitimate exchange of medical and scientific information during the development of a medicine. Grünenthal agreed to support this financially and without editorial control.

The pharmacist subsequently collated his data and asked a health economy liaison manager at Grünenthal a couple of questions about Versatis. Grünenthal helped with the printing of the poster and submission to the British Pain Society (BPS). The poster was peer reviewed by the Scientific Programme Committee and accepted.

Limited data was provided by Grünenthal which did not have editorial control.

A declaration appeared on the bottom of the full sized poster (which was several times bigger than the item at issue) that the item was 'Sponsored by an unrestricted educational grant by Grünenthal Ltd'. A similar declaration appeared at the bottom of the item in question, being an identical but smaller representation of the poster.

The poster was displayed in the poster session of the BPS independent congress meeting (13-15 April in Manchester). It was intended that the item at issue (the handout) would be available under the poster for delegates to take a copy. However, due to the poor print quality, the handout was removed before the congress opened and never used.

The item had never been sent out by medical information and nor had it been used proactively or reactively by any Grünenthal staff.

With respect to Clause 2, the item was developed to support a poster at an independent national congress. It was never used and so there could be no discredit upon the pharmaceutical industry.

In relation to Clause 3.2, the item was produced as part of the legitimate exchange of medical and

scientific information during the development of a medicine and complied with this clause. The item was never intended or used for promotion and had never been used.

Finally concerning Clause 9.1, high standards had been maintained by the intention of limiting the use of this item to the congress's medical and scientific poster session. In the end, it was never used, and certainly not for promotion.

In response to a request for further information Grünenthal stated that the handout was A3 in size. It was common practice to provide a reprint of a poster presentation at a scientific conference. Organisers often requested reprints from poster presenters. In line with this process, Grünenthal thus printed a number of handouts which, apart from size, were identical to the poster.

PANEL RULING

The Panel noted that Grünenthal had paid for the printing of the poster and had helped with its submission to the BPS; the company stated that it had not had editorial control of the poster. A consultant pharmacist appeared to have led on the development of the poster. The Panel did not know if the consultant pharmacist had been paid by Grünenthal in relation to the poster or had been otherwise retained by the company. A Grünenthal employee had provided information for the poster and was named as the second author although her position with Grünenthal was not declared. The Panel considered it was unacceptable of Grünenthal not to make it clear in its response that one of its employees was named as an author. The Panel considered that given that one of the named authors was a Grünenthal employee, the company could not dissociate itself from the content of the poster. It was difficult to see how in these circumstances Grünenthal could submit it had no editorial control.

The Panel noted that the material provided by the complainant was not the same size as either the poster or the handout; in that regard the material submitted could be a reproduction of either. The complainant had highlighted the phrase 'Versatis has an "off-label" use for the symptomatic relief of localised neuropathic pain, and could provide a substantial saving to the local health-economy'. In the Panel's view this was clearly a complaint about that sentence which appeared on the poster and the handout; it decided to consider the two items separately.

The Panel then considered whether the poster formed part of the legitimate exchange of medical and scientific information during the development of a medicine as submitted by Grünenthal. The certificate showed that the company had purported to approve it as promotional material. The Panel noted that the poster reported the outcome of a retrospective analysis of published literature (after 2000) on the treatment options for localised neuropathic pain. Electronic prescribing data from a primary care trust with a patient population of 500,000 was used as a basis of assumptions for the algorithm. The poster stated that recent literature showed that '…only 1% of PHN patients are prescribed Versatis patches first-line for PHN pain' and approximately 5% of patients trialled on gabapentin and pregabalin tried Versatis as second line. From this the authors predicted that 143 patients from a population of 500,000 would benefit from Versatis in PHN.

The results section referred to prescribing Versatis for the symptomatic relief of localised neuropathic pain and quantified the yearly savings that could be made by using Versatis compared with the cost of gabapentin at 3.6g/day or pregabalin.

The discussion section referred to the challenges of treating neuropathic pain in part due to its multiple aetiologies, symptoms and underlying mechanisms. The review highlighted the various pharmacological options for symptomatic treatment of localised neuropathic pain. It was stated that Versatis was an equitable option for pain management competing with gabapentin and pregabalin as a cost-effective choice and provided a saving to the local health-economy.

The Panel did not consider that the subject of the poster, the cost implications of prescribing Versatis in an unlicensed indication, contributed to the legitimate exchange of medical and scientific information during the development of a medicine as meant by the supplementary information to Clause 3, Marketing Authorization. The Panel queried whether the information presented contributed to the development of the medicine as it could be argued that the information was neither scientific nor medical. In the Panel's view discussion of unlicensed indications was more likely to be seen as promotional when products were already available on the market albeit for different indications. Taking all the circumstances into account the Panel did not consider that the poster could claim the benefit of the exemption in the supplementary information to Clause 3, Marketing Authorization. In the Panel's view the poster advocated using Versatis for localised neuropathic pain instead of gabapentin or pregabalin solely on the basis of cost. The poster also included a section 'Potential Costing Savings (for PHN)'. The Panel noted that treatment of PHN, a specific type of neuropathic pain, was within the Versatis marketing authorization.

The Panel examined the abstract for the poster. This was different to the poster in a number of ways. For example, the abstract clearly stated that a named person was a health economy liaison manager, Grünenthal. Unlike the poster the abstract did not mention the 'off-label' use of Versatis. It was stated in the abstract that the pharmacist and his colleague (the second author named in the abstract and named as third author on the poster/handout) 'received and [sic] educational grant from

Grünenthal Ltd for the development of the algorithm'. The poster included a copy of the algorithm, supporting statements, costing estimates and potential cost savings for PHN which were not included in the abstract. The abstract had four references 1-4. The poster cited these four references, listed 1-4, plus another set of references separately numbered 1-29.

The Panel considered that given Grünenthal's role in the production of the poster and its content it was promotional material and thus covered by the Code. The claim at issue promoted Versatis for an unlicensed indication and thus the Panel ruled a breach of Clause 3.2. The Panel considered that high standards had not been maintained and ruled a breach of Clause 9.1.

The Panel noted that Clause 2 was a sign of particular censure and reserved for such use. The Panel noted its comments above. The Panel was especially concerned that the company had certified the promotional item which referred to an unlicensed indication knowing that it would appear as part of a peer-reviewed poster presentation at a scientific conference. The Panel considered that delegates would be likely to view the material and the statement at issue differently if they knew it was promotional material. It considered that taking all the circumstances into account in this instance the company's activities reduced confidence in the pharmaceutical industry and thus ruled a breach of Clause 2.

The Panel noted Grünenthal's submission that the handout had not been used. In the circumstances the Panel ruled no breach of Clauses 2, 3.2 and 9.1.

Complaint received **5 July 2010**

Case completed **19 August 2010**

CASE AUTH/2331/7/10

NOVO NORDISK v LILLY

Promotional meeting

Novo Nordisk alleged that a meeting organised by Lilly, 'Treating Type 2 Diabetes - What Are Our Options?', promoted Byetta (exenatide) off-licence, misled the audience in terms of its licensed clinical use and did not encourage its rational use. According to the invitation an external health professional would cover the topic of pre-diabetes and the 'evidence on how best to manage' the condition. Novo Nordisk noted the prominent Byetta logo on the front of the invitation and the prescribing information on the back and strongly believed that a presentation and discussion on pre-diabetes was inappropriate and implied a wider indication for Byetta than its licensed indication.

Although the logos of Lilly and Amylin were displayed, and the prominent Byetta trademark suggested that the meeting would discuss Byetta, Novo Nordisk did not believe the declaration of sponsorship was sufficiently prominent from the outset. It was not clear whether Amylin had sponsored the meeting. Further, the declaration itself was not sufficiently detailed as to reflect the nature of each company's involvement in the meeting.

Given the above, and the fact that the invitation did not provide a clear indication as to the content or the form of the meeting and that there were spelling mistakes, Novo Nordisk believed high standards had not been maintained.

The detailed response from Lilly is given below.

The Panel noted that the invitation was accompanied by a letter on Lilly headed notepaper which described the meeting as promotional and sponsored by Lilly. The Panel also noted that Lilly accepted that the meeting was promotional in nature.

The Panel noted that the presentation at issue discussed, *inter alia*, the causes, diagnosis and management of pre-diabetes. The only reference to antidiabetic medicines was a bullet point on one slide which read 'Meds?? Metformin?? Glitazone????'. The Panel accepted that the presentation was informative and likely to have addressed delegates' educational needs. Nonetheless, it was an integral part of a promotional meeting; this was certainly the clear impression given by the invitation which bore the Byetta logo and included prescribing information. In the Panel's view, both recipients of the invitation and delegates would inevitably associate Byetta with pre-diabetes. The presentation was likely to prompt questions about the treatment of pre-diabetes with Byetta. The Panel considered that the presentation on pre-diabetes, as an integral part of a Byetta promotional meeting, meant that the promotion of Byetta was inconsistent with its marketing authorization. A breach of the Code was ruled. The invitation and meeting were misleading about Byetta's licensed indication and consequently did not encourage its rational use. Breaches of the Code were ruled.

The Panel noted that the supplementary information to the Code required the declaration of sponsorship to be sufficiently prominent such that readers of sponsored material were aware of it at the outset. The Panel considered that from the outset anyone receiving an invitation could be under no doubt that the promotional meeting to which they were being invited was organised by Lilly. No breach of the Code was ruled on this point.

It was not clear from the front page of the invitation why the Amylin corporate logo appeared. The Panel noted Lilly's submission that it indicated ownership of the product copyright. The only explanation appeared on the outside back cover beneath the prescribing information which stated that Byetta was a trademark of Amylin Pharmaceuticals Inc. Lilly submitted that Amylin had no role in Lilly's activities in the UK. The Panel considered that from the inclusion of the Amylin logo without explanation, potential delegates might assume that Amylin had some role in the arrangements and that was not so. Readers would not know from the outset that Amylin was a pharmaceutical company. However Amylin had not sponsored the meeting as it had no role whatsoever. The Panel considered that the position could have been made clearer but Lilly had not failed to meet the requirements of the Code; no breach was ruled.

The Panel did not consider that the invitation itself failed to meet high standards due to its content and spelling mistake as alleged. No breach was ruled.

Novo Nordisk Limited complained about a promotional meeting organized by Eli Lilly and Company Limited. Inter-company dialogue had failed to resolve matters.

COMPLAINT

Novo Nordisk stated that Lilly had organised a promotional meeting for 7 July 2010 entitled 'Treating Type 2 Diabetes - What Are Our Options?'. According to the four page invitation (ref UKBYT00414) an external health professional would cover the topic of pre-diabetes. The invitation stated this presentation would cover the 'evidence on how best to manage' the condition.

Novo Nordisk considered that the meeting promoted Byetta (exenatide), given the prominent Byetta logo on the front of the invitation and the prescribing information for it on the back. Byetta was a reasonable therapeutic choice for the treatment of pre-diabetes (Rosenstock *et al* 2010). However the current licensed indication for Byetta was the treatment of type 2 diabetes mellitus, when used in combination with metformin and/or a sulphonylurea.

Novo Nordisk strongly believed that a presentation and discussion on pre-diabetes was inappropriate at a Byetta promotional meeting and implied a wider indication for the medicine than its licensed indication. Novo Nordisk alleged that the meeting promoted Byetta off-licence, misled the audience in terms of its licensed clinical use and did not encourage its rational use in breach of Clauses 3.2, 7.2 and 7.10 of the Code.

Novo Nordisk also believed the declaration in relation to Lilly's involvement in this meeting was not sufficiently prominent. Although the logos of Lilly and Amylin were displayed on page 1 of the invitation, which implied these companies were involved in the meeting, and the Byetta trademark was extremely prominent on page 1, which suggested that the meeting would discuss Byetta, there was no declaration regarding the input of either of these companies on page 1, and as such Novo Nordisk did not believe the declaration was sufficiently prominent from the outset in breach of Clause 9.10.

In relation to the declaration of sponsorship on page 2, Novo Nordisk believed the location of the declaration and use of a smaller font size than the font size used in the main body of the invitation on page 2 constituted a further breach of Clause 9.10, as it was not sufficiently prominent.

Further, the declaration on page 2 'This meeting is organised by Eli Lilly and Company Limited' did not provide sufficient clarity as to the input of Lilly and Amylin in relation to this meeting. The declaration did not refer to Amylin's involvement; although the Amylin logo was displayed at the foot of pages 1 and 2 it was not clear whether Amylin had sponsored the meeting. Novo Nordisk alleged a breach of Clause 9.10.

Novo Nordisk considered that the declaration itself did not provide sufficient information as to the involvement of Lilly and Amylin in terms of the meeting content. Had they merely sponsored the meeting, or had they produced the actual content? As such, Novo Nordisk believed this constituted a further breach of Clause 9.10.

Given the above, and the fact that the invitation itself did not provide a clear indication as to the content, or the form of the meeting (the agenda only listed two presentations and a closing by the chairman, whereas the short description implied 'opportunity to discuss'…'arena to discuss'…'share learning'), and there were spelling mistakes with regard to the venue, Novo Nordisk believed high standards had not been maintained in breach of Clause 9.1.

RESPONSE

Lilly explained that the meeting was organised by its local diabetes representative. The context, content, supporting materials and overall arrangements were consistent with the requirements of Clause 19 and ensured an appropriate balance between diabetes related education and the promotion of Byetta, which had a marketing authorization for the treatment of patients with type 2 diabetes mellitus who were already receiving metformin and/or a sulphonylurea.

The agenda was developed by Lilly in consultation with a recognised local thought-leader in diabetes. The representative asked him to suggest a topic which would be of interest and relevant to his peers which he could then present at the meeting; he considered pre-diabetes to be a suitable educational topic. Lilly also solicited interest from another local health professional to support the other topic, identified by Lilly, which involved the promotion of Byetta. As a consequence, the meeting was entitled 'Treating Type 2 Diabetes – What Are Our Options?'

The potential delegates were identified by the representative and invited on the basis of their interest in the management of diabetes in primary care and therefore included GPs, pharmacists, practice nurses and diabetic specialist nurses. The potential delegates were limited to health professionals and appropriate administrative staff in accordance with the requirements of the Code.

The representative sent the meeting invitation with a letter (on Lilly letterhead) which she had signed. The letter clearly and prominently indicated that the invitation was to a professional meeting sponsored (organised) by Lilly. The invitation was therefore clearly promotional and included the Byetta product logo and branding, incorporated the Byetta prescribing information and the Lilly and Amylin corporate logos. The invitation further stated and clarified, on page 2, that 'This meeting is organised by Eli Lilly and Company Limited'. Given the promotional nature of the meeting this statement clearly left no doubt in the reader's mind as to Lilly's role in its organisation and administration.

Only the first paragraph of the 'invitation' section, on page 2 of the invitation (which began with the words 'This meeting will give you…'), related to the presentation on pre-diabetes. The subsequent two paragraphs referred to the treatment of type 2 diabetes and the role of Byetta.

The Amylin logo was included on the invitation because Byetta was a trade mark of Amylin Pharmaceuticals Inc; however all the UK marketing rights were held by Lilly. The European Marketing

Authorization holder was Eli Lilly Nederland BV. Amylin therefore had no role in Lilly's activities in the UK.

The speaker was briefed to give a scientific presentation discussing the relevance of pre-diabetes in primary care. This briefing expressly required that he should not mention any Lilly products. His presentation concentrated on causes and associations with pre-diabetes, screening procedures, diagnosis and potential prevention. The presentation included forty-four slides within which the fourth bullet point on slide 41 questioned whether 'metformin' or glitazones' had a role in the management of this condition; Lilly did not have a marketing authorization for either of these products in the UK. The wording 'Meds??' was also included in this slide but obviously was a generic mention. The representative was present at the meeting and confirmed that there was no mention of Byetta during this talk. The slides were, of course, reviewed and approved by Lilly in advance of the meeting. A copy of the presentation was provided.

Whilst the invitation and agenda promoted Byetta, the content and context of this particular section of the meeting genuinely attempted to address the educational requirements of the audience and did not support, invite or suggest the use of glucagon-like peptide-1 (GLP-1) receptor agonists such as Byetta or liraglutide in the management of pre-diabetes.

In summary, Lilly submitted that its role in organising this meeting was clear. It rejected Novo Nordisk's allegations that the presentation, or the meeting as a whole, was in breach of the Code. The company denied breaches of Clauses 3.2, 7.2, 7.10, 9.1 and 9.10.

Lilly was cognisant of its responsibilities with respect to the Code and had ensured that the promotional activities of its representatives were consistent with this (including, without limitation, Clauses 3.2, 7.2, 7.10, 9.1 and 9.10) and of the highest standard and quality.

PANEL RULING

The Panel noted that Byetta was indicated for treatment of type 2 diabetes mellitus in combination with metformin and/or sulphonylureas in patients who had not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.

The front page of the invitation featured the meeting title 'Treating Type 2 Diabetes – What Are Our Options?' above details of the chair, speakers, timings and venue. Beneath these logistical details in very small font size appeared the statement 'To access a wide range of information and resources to support both you and your patients, please visit: www.lillydiabetes.co.uk'. The Byetta product logo appeared prominently in the bottom right hand corner. The corporate logos for Lilly and Amylin appeared in the bottom left hand corner.

The inside front cover of the invitation, page 2, began 'This meeting will give you the opportunity to discuss Pre-Diabetes' and referred to its incidence, diagnosis and management. The introduction continued referring to how and when to use newer licensed medicines for type 2 diabetes. A detailed agenda appeared on page 3. There were two clinical presentations; the presentation at issue, 'Pre-Diabetes: There's a lot of it about' and 'Treating Type 2 Diabetes – What are Our Options?'. The Lilly and Amylin corporate logos appeared in the bottom right and left hand corners of pages 2 and 3 respectively. The statement 'This meeting is organised by Eli Lilly and Company Limited' appeared at the bottom of page 2 and prescribing information for Byetta appeared on the outside back cover. The back cover also contained the statement 'BYETTA (exenatide) is a trademark of Amylin Pharmaceuticals, Inc'.

The Panel noted that the invitation was accompanied by a letter on Lilly headed notepaper which described the meeting as promotional and sponsored by Lilly. The Panel also noted that Lilly accepted that the meeting was promotional in nature.

The Panel noted that the presentation at issue discussed the condition of pre-diabetes in relation to, *inter alia*, its causes, diagnosis and management. The management section discussed the prevention and treatment of pre-diabetes. The only reference to antidiabetic medicines was a bullet point on one slide which read 'Meds?? Metformin?? Glitazone????'. Other bullet points on the same slide referred to diet, lipids – 'statin if needed'- aspirin (if positive cardiac history) and retinopathy screening. The Panel accepted that the presentation was informative and was likely to have addressed delegates' educational needs. Nonetheless, it was an integral part of a promotional meeting; this was certainly the clear impression given by the invitation which bore the Byetta logo prominently on the front cover and included prescribing information. In the Panel's view, both recipients of the invitation and delegates would inevitably associate Byetta with pre-diabetes. The presentation was likely to prompt questions about the treatment of pre-diabetes with Byetta. This was especially so given that treatment of pre-diabetes was the subject of published debate and delegates might be aware of this. Novo Nordisk had referred to Rosenstock *et al* (published in June 2010) which assessed Byetta, *inter alia*, in patients with pre-diabetes. The Panel considered that the presentation on pre-diabetes, as an integral part of a Byetta promotional meeting, meant that the promotion of Byetta was inconsistent with its marketing authorization. A breach of Clause 3.2 was ruled. The invitation and meeting were misleading about Byetta's licensed indication and consequently did not encourage its rational use. Breaches of Clauses 7.2 and 7.10 were ruled.

The Panel noted that the supplementary information to Clause 9.10 required the declaration of sponsorship to be sufficiently prominent such that readers of sponsored material were aware of it at the outset. The Panel considered that the nature of the material was relevant when deciding whether the requirements of Clause 9.10 and its supplementary information were satisfied. The Panel considered that from the outset anyone receiving an invitation could be under no doubt that the promotional meeting to which they were being invited was organised by Lilly. The letter which accompanied the invitation was particularly clear in that regard. The invitation, which the Panel noted must stand alone under the Code, bore Byetta prescribing information and the Lilly corporate and product logos featured prominently on the front page. More details of Lilly's role appeared on page 2 which stated that the meeting was organised by Eli Lilly. Whilst it would have been preferable if these details had appeared on the front cover in the particular circumstances of this case the Panel did not consider that recipients would consider the invitation to be anything other than for a promotional meeting organised by Lilly. No breach of Clause 9.10 was ruled on this point.

The Panel noted the allegation about the Amylin corporate logo on the front page and page 2 of the invitation. It was not clear from the front page of the invitation why the Amylin corporate logo appeared. The Panel noted Lilly's submission that it indicated ownership of the product copyright. The only explanation appeared on the outside back cover beneath the prescribing information which stated that Byetta was a trademark of Amylin Pharmaceuticals Inc. Lilly submitted that Amylin had no role in Lilly's activities in the UK. The Panel noted that it was Lilly's sole responsibility to ensure that the material, including the reference to Amylin, complied with the Code. The Panel considered that from the inclusion of the Amylin logo without explanation, potential delegates might assume that Amylin had some role in the arrangements and that was not so. Readers would not know from the outset that Amylin was a pharmaceutical company. However Amylin had not sponsored the meeting as it had no role whatsoever. The Panel considered that the position could have been made clearer but Lilly had not failed to meet the requirements of Clause 9.10 and thus no breach was ruled in that regard.

The Panel did not consider that the invitation itself failed to meet high standards due to its content and spelling mistake as alleged. No breach of Clause 9.1 was ruled.

Complaint received **9 July 2010**

Case completed **6 September 2010**

CASE AUTH/2332/7/10

ANONYMOUS v GRÜNENTHAL

Versatis poster presentation

An anonymous and non-contactable complainant complained about a poster entitled 'Localised Neuropathic Pain' which referred to the use of Versatis (lidocaine plaster), a product supplied by Grünenthal. At the base of the poster in small type was 'Sponsored by an unrestricted educational grant by Grünenthal UK Ltd'.

Versatis was indicated for the symptomatic relief of neuropathic pain associated with previous herpes zoster infections (post-herpetic neuralgia, PHN).

The complainant stated that: 'The enclosed poster is being used currently by our field-based teams at Grünenthal to promote the off-label use of versatis [sic]. Not only that, but the poster was written by employees of Grünenthal, a fact which is not acknowledged on the poster, and the cost comparison analysis is flawed and misleading'.

In its detailed response, given below, Grünenthal explained that the item provided by the complainant had the same copy as a poster submitted to the poster session of a meeting of the British Pain Society (BPS) and the accompanying handout.

The Panel noted that the material in this case was the same as that considered in Case AUTH/2330/7/10. The Panel noted that Grünenthal had paid for the printing of the poster and had helped with its submission to the BPS; the company stated that it had not had editorial control of the poster. A consultant pharmacist appeared to have led on the development of the poster. The Panel did not know if the consultant pharmacist had been paid by Grünenthal or had been otherwise retained by the company. A Grünenthal employee had provided information for the poster and was named as the second author although her position with Grünenthal was not declared. The Panel considered it was unacceptable of Grünenthal not to make it clear in its response that one of its employees was named as an author. The Panel considered that given that one of the named authors was a Grünenthal employee, the company could not dissociate itself from the content of the poster. It was difficult to see how in these circumstances Grünenthal could submit it had no editorial control.

The Panel noted that in Case AUTH/2330/7/10 it had decided that given Grünenthal's role in the production of the poster and its content, it was promotional material and thus covered by the Code. The Panel considered that this decision also applied to this case, Case AUTH/2332/7/10.

The Panel noted Grünenthal's submission that the poster had only been used at the BPS meeting and that it had not been used elsewhere. The Panel also noted that the handout had been prepared for the BPS meeting but had not been used. The handout had not been used either proactively or reactively by any Grünenthal staff.

The complainant alleged that the poster was being used by Grünenthal field-based staff to promote the off-label use of Versatis. This was denied by Grünenthal. There was no evidence that the poster was being used by Grünenthal field-based staff and in that regard the Panel ruled no breach of the Code. Following its consideration of this allegation the Panel noted that the use of the poster had been considered in Case AUTH/2330/7/10 and a breach had been ruled as the Panel considered that a claim promoted the product for an unlicensed indication.

Turning back to the case now before it, the Panel then considered the allegations about the failure to acknowledge that one of the authors was a Grünenthal employee and about the cost comparison in relation to the poster displayed at the BPS.

The cost comparison analysis had not been considered in the previous case. The Panel noted that the cost comparison chart gave the daily, monthly and yearly costs per patient for gabapentin 1800mg/day, pregabalin 600mg/day and Versatis 1 patch/day. It appeared to the Panel that there were errors in the calculations.

The Panel also queried the choice of dose for each medicine in that, *inter alia*, it appeared that the costs were based on the maximum dose of pregabalin but not the maximum dose of Versatis or gabapentin as Neurontin. The poster had no data or mention about how the doses compared clinically. It suggested increasing the dose of gabapentin to 3600mg per day which was outside the licensed dose for at least one form of gabapentin (Winthrop). Further the Neurontin (gabapentin (Pfizer))SPC stated that in the treatment of peripheral neuropathic pain such as painful diabetic neuropathy and PHN, efficacy and safety had not been examined in clinical treatment periods longer than 5 months. If a patient required dosing for longer than 5 months the physician should assess the patient's clinical status and determine the need for additional therapy.

The cost comparison used the symbol * next to Versatis but no explanation was given.**

The Panel examined the algorithm which appeared

in the poster and again noted arithmetic mistakes. It was not clear whether the costs in the algorithm were taken from the cost comparison chart or *vice versa*. The Panel also queried the algorithm in that the data for gabapentin and pregabalin took account of patients changed to other therapies whereas all the Versatis patients continued with that medication. The algorithm did not mention the doses of the various medicines.

The Panel considered that the cost comparison was inaccurate and misleading. A breach of the Code was ruled. High standards had not been maintained in relation to the content of the poster and a breach was ruled.

The Panel noted that the employment status of the second author had not been clearly stated. In the Panel's view readers should have been able to view the poster knowing that the second author was a Grünenthal employee. The Panel considered that high standards had not been maintained in this regard and ruled a breach.

The Panel noted that Clause 2 was a sign of particular censure and reserved for such use. The Panel noted its decision that the poster was promotional material for which Grünenthal was responsible. The Panel noted its critical comments on the content of the poster and its ruling of a breach. The Panel was concerned that Grünenthal had certified the poster as promotional material knowing that it was to be displayed at the scientific poster session of the BPS Congress. The employment status of the second author had not been disclosed. Overall, the Panel considered that the company's activities reduced confidence in the pharmaceutical industry and thus ruled a breach of Clause 2.

An anonymous and non-contactable complainant complained about a poster entitled 'Localised Neuropathic Pain' which referred to the use of Versatis (lidocaine plaster), a product supplied by Grünenthal Ltd. At the base of the poster in small type was 'Sponsored by an unrestricted educational grant by Grünenthal UK Ltd'.

Versatis was indicated for the symptomatic relief of neuropathic pain associated with previous herpes zoster infections (post-herpetic neuralgia, PHN).

COMPLAINT

The complainant stated that: 'The enclosed poster is being used currently by our field-based teams at Grünenthal to promote the off-label use of versatis [sic]. Not only that, but the poster was written by employees of Grünenthal, a fact which is not acknowledged on the poster, and the cost comparison analysis is flawed and misleading'.

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

RESPONSE

Grünenthal explained that the item was not a poster but was intended for use as a handout at the British Pain Society (BPS) poster exhibition. It was not being used by any Grünenthal staff and had never been used. The item was not written by Grünenthal and it acknowledged the support given, not editorial involvement.

In relation to the cost comparison, the poster itself (of which the item in question was intended as a handout) was written by the authors. The main author supplied further justification for the Panel.

Original references were provided. There were two listings and some citations were duplicated. Some were the authors' own calculations. Only some of the references were used in the poster. This was again evidence that Grünenthal did not have editorial control.

Grünenthal explained that a consultant pharmacist and his colleague had an informal discussion with the Grünenthal market access director about the pharmacist's local health economic data and getting it 'published'. As part of the legitimate exchange of medical and scientific information during the development of a medicine, Grünenthal agreed to support this financially and without editorial control. This led to the pharmacist collating his data and asking a health economy liaison manager working for Grünenthal a couple of questions about Versatis. Grünenthal helped with the printing of the poster and submission to the BPS. The poster was peer reviewed by the BPS Scientific Programme Committee and accepted.

A declaration appeared on the bottom of the full sized poster (which was several times bigger than the item at issue) that the poster was 'Sponsored by an unrestricted educational grant by Grünenthal Ltd'. A similar declaration appeared at the bottom of the item in question, being an identical but smaller representation of the poster.

The poster was displayed in the poster session of the BPS independent congress meeting (13-15 April in Manchester). The intention was that the item at issue (the handout) would be available under the poster for delegates to take a copy. However, due to the poor print quality, the handout was removed before the congress opened and never used.

The item had never been sent out by medical information and nor had it been used proactively or reactively by any Grünenthal staff. It was never approved for promotional use. It was certified as a poster handout.

Limited data was provided by Grünenthal but no-one in Grünenthal had editorial control.

With respect to Clause 2, this item was developed to support a poster at an independent national congress. It was never used and so there could be

no discredit upon the pharmaceutical industry.

In relation to Clause 3.2, this item was produced a part of the legitimate exchange of medical and scientific information during the development of a medicine and complied with this clause. The item was never intended or used for promotion. Again, it had never been used.

With regard to Clause 7.2 Grünenthal provided details of the production of the algorithm. It also noted that this was also a peer reviewed abstract reviewed by the BPS Scientific Programme Committee. Clause 7.2 had not been breached.

Finally concerning Clause 9.1, Grünenthal submitted that high standards had been maintained by the intention of limiting the use of this item to the congress' medical and scientific poster session. In the end, it was never used, and certainly not for promotion.

Grünenthal was concerned that this malicious complaint had apparently been made by one of its employees (since this item was never made available outside of Grünenthal) and that this was yet another anonymous, non-contactable complaint about the company. At least in this instance Grünenthal had evidence it could identify and refute any breaches of the Code.

In response to a request for more information, Grünenthal confirmed that the further information requested by the Panel in Case AUTH/2330/7/10 could be used in this case ie Grünenthal stated that the handout was A3 in size. It was common practice to provide a reprint of a poster presentation at a scientific conference. Organisers often requested reprints from poster presenters. Grünenthal thus printed a number of handouts which, apart from size, were identical to the poster.

In response to a further request for more information Grünenthal confirmed that the poster had only been used at the BPS meeting in April and no further use had been made of it. No-one at Grünenthal had been provided with copies of the poster.

PANEL RULING

The Panel noted that the material in this case was the same as that considered in Case AUTH/2330/7/10. The Panel noted that Grünenthal had paid for the printing of the poster and had helped with its submission to the BPS; the company stated that it had not had editorial control of the poster. A consultant pharmacist appeared to have led on the development of the poster. The Panel did not know if the consultant pharmacist had been paid by Grünenthal or had been otherwise retained by the company. A Grünenthal employee had provided information for the poster and was named as the second author although her position with Grünenthal was not declared. The Panel considered it was unacceptable of Grünenthal not to make it clear in its response that one of its employees was named as an author. The Panel considered that given that one of the named authors was a Grünenthal employee, the company could not dissociate itself from the content of the poster. It was difficult to see how in these circumstances Grünenthal could submit it had no editorial control.

The Panel noted that in Case AUTH/2330/7/10 it had decided that given Grünenthal's role in the production of the poster and its content it was promotional material and thus covered by the Code. The Panel decided that this decision also applied to the present case, Case AUTH/2332/7/10.

The Panel noted Grünenthal's submission that the poster had only been used at the BPS meeting in April and that it had not been used elsewhere. The Panel also noted that the handout had been prepared for the BPS meeting but had not been used. The handout had not been used either proactively or reactively by any Grünenthal staff.

The complainant alleged that the poster was being used by Grünenthal field-based staff to promote the off-label use of Versatis. This was denied by Grünenthal. There was no evidence that the poster was being used by Grünenthal field-based staff and in that regard the Panel ruled no breach of Clauses 2, 3.2, 7.2 and 9.1. Following its consideration of this allegation the Panel noted that the use of the poster had been considered in Case AUTH/2330/7/10 and a breach of Clause 3.2 had been ruled as the Panel considered that a claim promoted the product for an unlicensed indication.

Turning back to the case now before it, the Panel then considered the allegations about the failure to acknowledge that one of the authors was a Grünenthal employee and about the cost comparison in relation to the poster displayed at the BPS.

The cost comparison analysis had not been considered in the previous case. The Panel noted that the cost comparison chart gave the daily, monthly and yearly costs per patient for gabapentin 1800mg/day, pregabalin 600mg/day and Versatis 1 patch/day.

It appeared to the Panel that there were errors in the calculations as the daily cost of gabapentin (£1.23) would give a monthly cost of £34.44 and not £34.49 as given in the chart. This daily cost would give an annual cost of £447.72 and not £448.38 as given in the chart. Similar errors were made for Versatis in that based on the daily cost of £2.41 the monthly cost should be £67.48 and yearly cost £877.24 not £67.57 and £878.45 respectively as given in the chart.

The Panel queried the choice of dose. It appeared from the Versatis summary of product characteristics (SPC) that the maximum recommended dose was three plasters applied simultaneously for 12 hours (Section 5.2). The subsequent plaster free interval must be at least 12

hours (Section 4.2 of the SPC). Pregabalin for neuropathic pain could be given at a maximum dose of 600mg/day (Lyrica SPC). Gabapentin for neuropathic pain could be given at a daily maximum of 3600mg (Neurontin SPC (Pfizer)) but only the cost of the 1800mg/day dose was detailed in the poster. The Neurontin SPC stated that in the treatment of peripheral neuropathic pain such as painful diabetic neuropathy and PHN, efficacy and safety had not been examined in clinical treatment periods longer than 5 months. If a patient required dosing for longer than 5 months the physician should assess the patient's clinical status and determine the need for additional therapy.

It appeared that the costs were based on the maximum dose of pregabalin but not the maximum dose of Versatis or gabapentin as Neurontin. The poster had no data or mention about how the doses compared clinically. It suggested increasing the dose of gabapentin to 3600mg per day which was outside the licensed dose for at least one form of gabapentin (Winthrop).

The cost comparison used the symbol *** next to Versatis but no explanation was given.

The Panel examined the algorithm which appeared in the poster. It noted that 3300 patients with persistent localised neuropathic pain needed long term prescribing of medicines. The algorithm allocated 70% of patients to gabapentin (2145 patients) whereas 70% of 3300 was 2310. (This figure had been corrected on the material submitted by Grünenthal to substantiate the poster). Of the patients on gabapentin 80% would continue long term giving an overall figure of 1716 on the poster whereas 80% of 2310 was 1848. (This figure had been corrected on the material submitted by Grünenthal to substantiate the poster). Thus the algorithm was incorrect. It was not clear whether the costs in the algorithm were taken from the cost comparison chart or *vice versa*. The Panel also queried the algorithm in that the data for gabapentin and pregabalin took account of patients changed to other therapies whereas all the Versatis patients continued with that medicine. The algorithm did not mention the doses of the various medicines.

The Panel considered that the cost comparison was not accurate and was misleading. A breach of Clause 7.2 was ruled. High standards had not been maintained in relation to the content of the poster and a breach of Clause 9.1 was ruled.

The Panel noted that the employment status of the second author had not been clearly stated. In the Panel's view readers should have been able to view the poster knowing that the second author was a Grünenthal employee. The Panel considered that high standards had not been maintained in this regard and ruled a breach of Clause 9.1.

The Panel noted that Clause 2 was a sign of particular censure and reserved for such use. The Panel noted its decision that the poster was promotional material for which Grünenthal was responsible. The Panel noted its critical comments on the content of the poster and its ruling of a breach of Clause 7.2. The Panel was concerned that Grünenthal had certified the poster as promotional material knowing that it was to be displayed at the scientific poster session of the BPS Congress. The employment status of the second author had not been disclosed. It considered that taking all the circumstances into account in this instance the company's activities reduced confidence in the pharmaceutical industry and thus ruled a breach of Clause 2.

Complaint received **12 July 2010**

Case completed **19 August 2010**

CASE AUTH/2334/7/10

NORGINE v MOVETIS

Promotion of Resolor

Norgine complained about the promotion of Resolor (prucalopride) by Movetis (UK) Limited. The material at issue, was a folder, a leavepiece and a drop card each of which contained the claim, 'At last! A new way out of chronic constipation in women'. Resolor was indicated for the symptomatic treatment of chronic constipation in women in whom laxatives failed to provide adequate relief.

Norgine alleged that the claim was not in accordance with the terms of the Resolor marketing authorization and was inconsistent with the summary of product characteristics (SPC). Resolor was not indicated for all women with chronic constipation, only those who failed to respond to laxatives. Norgine further alleged that the claim was misleading as it implied that Resolor was suitable for all women with chronic constipation and that was not so. And finally it exaggerated Resolor's properties by claiming that it was a 'A new way out of chronic constipation in women'. The claim was all embracing as it implied that Resolor was licensed and could be used for all cases of chronic constipation and that was not so.

In inter-company dialogue, Movetis had stated that it would ensure that all future promotional items clearly stated 'in whom laxatives fail to provide adequate relief'. Norgine noted, however that the same claim was made in material produced after the undertaking was given.

The detailed response from Movetis is given below.

The folder, leavepiece and drop card at issue all included the claim 'At last! A new way out of chronic constipation in women' beneath the most prominent mention of the brand name. This was immediately followed by a picture of a woman's stomach beneath which was the claim 'Resolor is indicated for symptomatic treatment of chronic constipation in women in whom laxatives fail to provide adequate relief'.

The Panel considered that any qualification necessary to ensure compliance with the Code should be part of the claim itself or appear prominently within the same visual field. The Panel considered each item separately as the context of claims could be a relevant factor.

With regard to the A4 folder, the Panel considered that the qualification that Resolor was to be used when laxatives had not provided adequate relief should have appeared as part of the claim itself or immediately beneath it. The size of the folder was relevant. The visual separation of the claim from its qualification by the illustration of the woman's stomach meant that the claim at issue was inconsistent with the SPC. The claim was also misleading about Resolor's licensed indication and did not promote its rational use; the claim could not stand alone without reference to another statement. Breaches of the Code were ruled.

With regard to the A5 leavepiece, the Panel noted that the layout was similar to the front of the folder. The qualification on page 1 was physically nearer to the claim at issue due to the smaller size of the item but again the claim and its qualifications were separated by the illustration. The physical separation was compounded by the fact that the qualification was in a smaller font size and less prominent font colour and background contrast than the claim at issue above. Further, page 3 of the leavepiece included the claim, omitting the phrase 'At last…' without any mention that the product could only be used when laxatives had failed to provide adequate relief. The Panel considered that the claim on both pages 1 and 3 was inconsistent with the SPC. Breaches of the Code were also ruled for the same reasons as with the folder.

The drop card consisted of two sides and was the size of a large bookmark. The claim at issue was again separated from its qualification by the illustration of the woman's stomach. In addition the qualification appeared as the first of a series of claims on the front of the drop card which were of identical font size and colour and thus as a group were clearly differentiated from the prominent claim at issue above. The claim at issue was thus inconsistent with the SPC. Breaches of the Code were ruled for the same reasons as with the folder.

Upon appeal by Movetis of all of the Panel's rulings of breaches of the Code, the Appeal Board noted that each item at issue was headed 'Resolor prucalopride. At last! A new way out of chronic constipation in women'. This claim was above a picture of a woman's stomach partially covered by the woman's hands which were angled downwards. Below the photograph was the second claim 'Resolor is indicated for symptomatic treatment of chronic constipation in women in whom laxatives fail to provide adequate relief'.

The Appeal Board noted that the cover of the A4 folder featured the claims and picture described above. The only other text was the Movetis corporate logo in the bottom right hand corner. The Appeal Board considered that with virtually no other text to distract a reader, the eye was drawn almost immediately from the headline claim to the

second claim. The Appeal Board thus did not consider that readers would be misled as to the licensed indication for Resolor and in its view the A4 folder promoted the rational use of the medicine. No breaches of the Code were ruled.

The Appeal Board noted that the front cover of the A5 leavepiece was closely similar to that of the A4 folder. The Appeal Board considered that its comments about the folder also applied to the front cover of the leavepiece. No breaches of the Code ruled.

The Appeal Board noted that when the leavepiece was opened out, the double page spread of pages 2 and 3 featured the product name and strapline 'A new way out of chronic constipation in women' at the bottom of page 3. To the right of that claim was the photograph of the woman's stomach and hands and to the right of that was that tagline 'Rx prucalopride 1-2mg od'. The Appeal Board noted that the claim 'A new way out of chronic constipation in women' was not qualified in any way and was followed by a very simple prescribing instruction. The Appeal Board was concerned that this was not sufficiently clear with regard to Resolor's indication that it was only for those women in whom laxatives had failed to provide adequate relief. The claim 'A new way out of chronic constipation' on page 3 was inconsistent with the SPC, misleading and did not promote rational use. The Appeal Board upheld the Panel's rulings of breaches of the Code.

With regard to the drop card, the Appeal Board noted that the top half featured the heading, photograph and second claim as previously described. Although the bottom half of the card featured a number of claims for Resolor the heading and the second claim were only separated by the photograph; there was no intervening text. The Appeal Board noted its comments and rulings above with regard to the A4 folder and considered that they also applied to the drop card. The Appeal Board ruled no breaches of the Code.

Norgine Pharmaceuticals Ltd complained about the promotion of Resolor (prucalopride) by Movetis (UK) Limited. The claim at issue was 'At last! A new way out of chronic constipation in women'. Resolor was indicated for the symptomatic treatment of chronic constipation in women in whom laxatives failed to provide adequate relief.

COMPLAINT

In inter-company dialogue, Norgine had alleged that the unqualified claim 'A new way out of chronic constipation in women' which appeared in a Resolor advertisement published in the BMJ, 28 April 2010, was not in accordance with the terms of the Resolor marketing authorization and was inconsistent with the summary of product characteristics (SPC) in breach of Clause 3.2. Resolor was not indicated for all women with chronic constipation, only those who failed to respond to laxatives. Secondly, the claim was misleading as it implied that Resolor was suitable for all women with chronic constipation and that was not so, in breach of Clause 7.2. And thirdly, it exaggerated the properties of Resolor by claiming that it was a 'A new way out of chronic constipation in women' in breach of Clause 7.10. The claim was all embracing as it implied that Resolor was licensed and could be used for all cases of chronic constipation and that was not so.

Norgine accepted (letter dated 14 May, 2010) Movetis' proposal that it would stop using the advertisement and any analogous items and its undertaking '… to ensure that all future promotional items clearly stated''in whom laxatives fail to provide adequate relief'''. Norgine informed Movetis that it considered that inter-company dialogue had been successful, but that if it were to see any future unqualified use of the indication it would proceed directly to a complaint to the Authority.

On 29 June, two of Norgine's representatives attended a Movetis satellite symposium at the Association of Coloproctology of Great Britain and Ireland meeting in Bournemouth, a folder (ref UK/RES/10/00013 June 2010); leavepiece (ref UK/RES/10/0005 June 2010) and a drop card (ref UK/RES/10/0004 June 2010) were picked up. All of the items contained the claim 'At last! A new way out of chronic constipation in women'. Norgine was very disappointed that despite the specific undertaking made to it as part of inter-company dialogue, the same claim was made in material that was produced after the undertaking was given. Norgine alleged that the material was in breach of Clauses 3.2, 7.2 and 7.10.

RESPONSE

Movetis stated that it understood that inter-company dialogue had successfully resolved the matter and it was, therefore, disappointed to receive this complaint sent directly to the Authority. Movetis firmly believed that it acted properly and in accordance with the Code and its undertaking to Norgine. All past and current items in the Resolor marketing campaign complied with the marketing authorization for the product.

An example of promotional material submitted to the Medicines and Healthcare products Regulatory Agency (MHRA) for pre-vetting (ref RES-0027), was provided, accompanied by the MHRA approval letter dated 6 November 2009. The tagline approved by the MHRA read: 'The new way out of chronic constipation'.

When Resolor was launched in the UK, 22 March 2010, the tagline had evolved to: 'At last! A new way out of chronic constipation in women'. This tagline was used in the BMJ advertisement (ref RES0140-UKv1) over which Norgine and Movetis had corresponded and formed the basis for Movetis' subsequent undertaking.

Movetis did not agree with Norgine that the claim 'A new way out of chronic constipation in women' was not adequately qualified but in the spirit of resolving issues through inter-company dialogue, it confirmed (letter dated 24 May) that: 'all other current and future UK promotional items will comply with our undertaking to include the full licensed indication'.

Movetis submitted that the correspondence with Norgine demonstrated that both parties acknowledged that they had reached a successful resolution of the matter (copies provided).

Movetis' interpretation of this undertaking was clear – that in addition to the claims on the advertisement (and all future promotional items) it would clearly provide the full indication. Movetis did not undertake to change, remove or amend any of the existing claims in the advertisement.

All of Movetis' current and subsequent materials, including the leavepiece, folder and drop card at issue in this case, bore the full licensed indication for Resolor clearly, prominently, in large font with no distracting copy or imagery surrounding the statement. In this regard Movetis was confident that it had fully complied with its undertaking.

In conclusion, and to reiterate, Movetis firmly believed that it acted properly and in accordance with the Code and its undertaking to Norgine.

PANEL RULING

The folder, leavepiece and drop card at issue all included the claim 'At last! A new way out of chronic constipation in women' beneath the most prominent mention of the brand name. This was immediately followed by a picture of a woman's stomach beneath which was the claim 'Resolor is indicated for symptomatic treatment of chronic constipation in women in whom laxatives fail to provide adequate relief'.

The Panel considered that any qualification necessary to ensure compliance with the Code should be part of the claim itself or appear prominently within the same visual field. The Panel considered each item separately as the context of claims could be a relevant factor.

With regard to the A4 folder, the Panel considered that the qualification that Resolor was to be used when laxatives had not provided adequate relief should have appeared as part of the claim itself or immediately beneath it. The size of the folder was relevant. The visual separation of the claim from its qualification by the illustration of the woman's stomach meant that the claim at issue was inconsistent with the SPC. A breach of Clause 3.2 was ruled. The claim was also misleading about Resolor's licensed indication and did not promote its rational use; the claim could not stand alone without reference to another statement. Breaches of Clauses 7.2 and 7.10 were ruled.

With regard to the A5 leavepiece, the Panel noted that the layout was similar to the front of the folder. The qualification on page 1 was physically nearer to the claim at issue due to the smaller size of the item but again the claim and its qualifications were separated by the illustration. The physical separation was compounded by the fact that the qualification was in a smaller font size and less prominent font colour and background contrast than the claim at issue above. Further, page 3 of the leavepiece included the claim, omitting the phrase 'At last…' without any mention that the product could only be used when laxatives had failed to provide adequate relief. The Panel considered that the claim on both pages 1 and 3 was inconsistent with the SPC. A breach of Clause 3.2 was ruled. Breaches of Clauses 7.2 and 7.10 were also ruled for the same reasons as with the folder.

The drop card consisted of two sides and was the size of a large bookmark. The claim at issue was again separated from its qualification by the illustration of the woman's stomach. In addition the qualification appeared as the first of a series of claims on the front of the drop card which were of identical font size and colour and thus as a group were clearly differentiated from the prominent claim at issue above. The claim at issue was thus inconsistent with the SPC. Breaches of Clauses 3.2, 7.2 and 7.10 were ruled for the same reasons as with the folder.

APPEAL FROM MOVETIS

Movetis submitted that it had acted properly and in accordance with its marketing authorization and with the Code for all past and current items in the Resolor marketing campaign. Similar items from its campaign were subject to MHRA pre-vetting and were considered acceptable. The items at issue were well within the boundaries of current standard industry practice and the practice of Movetis' peers, including those in the same therapeutic area.

The Code did not stipulate how or where images should be positioned within an item. The Panel referred to 'visual field' and 'visual separation', neither of which were defined or covered in the Code; these were subjective terms and open to interpretation without further guidance.

The items at issue bore the full licensed indication for Resolor, not asterisked as a small text footnote, but clearly, prominently, in large font, with no distracting copy or imagery surrounding the statement.

RESPONSE FROM NORGINE

Norgine concurred with the Panel's view that any qualification of a claim necessary to ensure compliance with the Code should be part of the claim itself or appear prominently within the same visual field. In this case the qualification of the claim necessary to comply with the indications for the

product was neither part of the claim itself nor did it appear prominently within the same visual field due to the considerable physical separation of the claim and its qualification in the materials in question; it was difficult to see how the claim and the qualification could have been separated more than they were.

The marketing authorization application initially proposed that Resolor should be indicated for the treatment of chronic constipation in adults in whom laxatives failed to provide adequate relief. After review of the dossier, the indication was revised and endorsed by the CHMP to the symptomatic treatment of chronic constipation in women in whom laxatives failed to provide adequate relief (ref Resolor, European Public Assessment Report, page 4).

Norgine alleged that it was clear that from the start of the marketing authorization process, the manufacturers considered that the more important qualification was the restriction in use of the product to patients in whom laxatives failed to provide adequate relief. The restriction to women only emerged during the licensing process.

Norgine therefore submitted that claims for this product would only comply with the Code if the full qualifications of the indication were part of the claims.

APPEAL BOARD RULING

The Appeal Board noted that each item at issue was headed 'Resolor prucalopride. At last! A new way out of chronic constipation in women'. This claim was above a picture of a woman's stomach partially covered by the woman's hands which were angled downwards. Below the photograph was the second claim 'Resolor is indicated for symptomatic treatment of chronic constipation in women in whom laxatives fail to provide adequate relief'.

The Appeal Board noted that the cover of the A4 folder featured the claims and picture described above. The only other text was the Movetis corporate logo in the bottom right hand corner. The Appeal Board considered that with virtually no other text to distract a reader, the eye was drawn almost immediately from the headline claim to the second claim. The Appeal Board thus did not consider that readers would be misled as to the licensed indication for Resolor and in its view the A4 folder promoted the rational use of the medicine. No breach of Clauses 3.2, 7.2 and 7.10 were ruled. The appeal was thus successful.

The Appeal Board noted that the front cover of the A5 leavepiece was closely similar to that of the A4 folder. The Appeal Board considered that its comments about the folder also applied to the front cover of the leavepiece. No breach of Clauses 3.2, 7.2 and 7.10 were ruled. The appeal on this point was thus successful.

The Appeal Board noted that when the leavepiece was opened out, the double page spread of pages 2 and 3 featured the product name and strapline 'A new way out of chronic constipation in women' at the bottom of page 3. To the right of that claim was the photograph of the woman's stomach and hands and to the right of that was that tagline 'Rx prucalopride 1-2mg od'. The Appeal Board noted that the claim 'A new way out of chronic constipation in women' was not qualified in any way and was followed by a very simple prescribing instruction. The Appeal Board was concerned that this was not sufficiently clear with regard to Resolor's indication that it was only for those women in whom laxatives had failed to provide adequate relief. The claim 'A new way out of chronic constipation' on page 3 was inconsistent with the SPC, misleading and did not promote rational use. The Appeal Board upheld the Panel's rulings of breaches of Clauses 3.2, 7.2 and 7.10. The appeal on this point was unsuccessful.

With regard to the drop card, the Appeal Board noted that the top half featured the heading, photograph and second claim as previously described. Although the bottom half of the card featured a number of claims for Resolor the heading and the second claim were only separated by the photograph; there was no intervening text. The Appeal Board noted its comments and rulings above with regard to the A4 folder and considered that they also applied to the drop card. The Appeal Board ruled no breach of Clauses 3.2, 7.2 and 7.10 of the Code. The appeal on this point was thus successful.

Complaint received **20 July 2010**

Case completed **2 November 2010**

CASE AUTH/2336/7/10

ANONYMOUS MEDICAL CONTRACTOR v GLAXOSMITHKLINE

Alleged unprofessional promotional practices

An anonymous and uncontactable medical contractor providing compliance services to pharmaceutical companies, including GlaxoSmithKline UK, alleged the following unprofessional practices within GlaxoSmithKline's respiratory and allergy therapy area:

1 Regular references to the regulatory authorities including the Medicines and Healthcare products Regulatory Agency (MHRA).

2 Use of the word 'new' for Avamys for more than a year.

3 No prescribing information for the products promoted on the health professional website.

4 Poor training of medical representatives and the setting of unrealistic targets for Rupafin, manipulating representatives into various target driven, unethical practices.

The detailed response from GlaxoSmithKline is given below.

The Panel noted that a Seretide leavepiece included the claim 'To aid compliance with the concomitant use of ICS [inhaled corticosteroid] and LABA [long-acting beta agonist], a combination inhaler should be used when appropriate (MHRA Drug Safety update)[4]'. Reference 4 given on the last page also referred to the MHRA as did reference 13 on the last page of the detail aid in support of a similar claim. The Panel thus ruled that the detail aid and the leavepiece were each in breach of the Code.

The Panel noted that promotion of Avamys started on 2 February 2009. An email instructing representatives to stop using current materials, sent on 4 February 2010 referred to immediately recalling certain items that no longer complied with the Code because of the use of the word 'new'. Material describing Avamys as new had not been recalled until 4 February 2010 and so in that regard it had been used for more than twelve months. Thus the Panel ruled a breach of the Code.

The Panel noted that with regard to the prescribing information on health professional websites the complainant had not provided any detail or examples of where prescribing information had not been provided. The Panel noted that material provided by GlaxoSmithKline showed that prescribing information was provided as a link on the website pages. On the basis of the information before it, the Panel ruled no breach of the Code.

The Panel noted that detailed training was provided for representatives promoting Rupafin. No breach of the Code was ruled.

The Panel noted GlaxoSmithKline's submission that its targets for representatives were ambitious but achievable. The Panel noted that no information had been provided by the complainant about what was unrealistic about the targets nor about the representatives' alleged target driven, unethical practices. The Panel decided that on the basis of the information before it there was no breach of the Code.

The Panel noted its rulings above and did not consider that overall GlaxoSmithKline had failed to maintain a high standard; no breach of the Code was ruled.

An anonymous and uncontactable medical contractor providing compliance services to pharmaceutical companies, including GlaxoSmithKline UK Ltd, complained about the promotional practices of GlaxoSmithKline.

COMPLAINT

The complainant stated that it would be a gross failure in the discharge of their professional duties if they failed to call to the Authority's attention the following unprofessional practices within GlaxoSmithKline's respiratory and allergy therapy area:

1 Regular references to the regulatory authorities including the Medicines and Healthcare products Regulatory Agency (MHRA) in all promotional items/materials for Seretide, Avamys, Rupafin and other branded products in the therapy area. This practice had been on-going since 2008 until the present.

2 Continued use of the word 'new' for Avamys despite it having been marketed for more than a year.

3 Non inclusion of prescribing information for the products promoted on the health professional website.

4 Poor training of medical representatives and the setting of unrealistic targets for Rupafin thereby placing commercial interests above ethics with the resultant manipulation of representatives into various target driven, unethical practices.

The complainant stated that this should be treated as an anonymous complaint, made in good faith to protect the reputation of the pharmaceutical companies and to protect public safety, as they

were currently contracted to GlaxoSmithKline where resistance to clinical governance and compliance remained very strong.

When writing to GlaxoSmithKline, the Authority asked it to respond in relation to Clauses 4.1, 7.11, 9.1, 9.5, 15.2, 15.4, 15.9 and 16.1 of the Code.

RESPONSE

GlaxoSmithKline noted that the introduction to the Constitution and Procedure stated:

> 'A complainant has the burden of proving their complaint on the balance of probabilities. Anonymous complaints are accepted and like all complaints are judged on the evidence provided by the parties. The weight to be attached to any evidence may be adversely affected if the source is anonymous and thus in some instances it will not be possible for such a complaint to proceed.'

GlaxoSmithKline asked the Authority to consider, given that no evidence was provided, whether it had a case to answer.

GlaxoSmithKline took its responsibility to ensure patient safety and compliance with all relevant ethical and regulatory codes very seriously and it strongly refuted any accusation that it had done otherwise. GlaxoSmithKline's proactive approach to compliance and its ethical stance was reflected in its record of inter-company and Authority complaints over the past few years.

GlaxoSmithKline had an open culture where the raising of ethical and compliance concerns was welcomed and where final signatories took their responsibilities very seriously. It was disappointed that someone employed to raise such concerns and to ensure compliance with the Code did not think it appropriate to do so directly with GlaxoSmithKline. A survey conducted in late 2009 indicated that the vast majority of employees understood what constituted ethical business practice and conduct in their job; considered that their working environment encouraged ethical behaviour, even in the face of pressures to meet business objectives, and that department leaders created an atmosphere of trust in which concerns could be raised.

Notwithstanding the above, in the spirit of the Code, GlaxoSmithKline responded to each of the points raised.

1 References to the regulatory authorities including the MHRA

GlaxoSmithKline refuted the allegation that all materials for Seretide, Avamys and Rupafin contained regular, or any other, references to regulatory agencies as evidenced by copies of currently used versions of the detail aids for each of the three products. Therefore GlaxoSmithKline denied a breach of Clause 9.5.

In the spirit of transparency, GlaxoSmithKline noted the following items:

- Reactive supplementary Seretide detail aid (ref SFL/DAP/09/42343/1) which featured the following claim: 'To aid Compliance with the concomitant use of inhaled corticosteroids and LABA [long-acting beta agonist], a combination inhaler should be used where appropriate'. This was supported by information provided in the publication 'Drug Safety Update' which was listed in the reference section as the 'MHRA Drug Safety Update. Volume 2, issue 12 July 2009'. This item was to respond to questions that might arise during a sales call.

- Seretide leavepiece (ref SFL/LVF/09/34470/2) where the same publication (Drug Safety Update) was listed within the body of the item as the 'MHRA Drug Safety Update'. This item was withdrawn 17 September 2009, two months after release due to the inclusion of 'MHRA' within the body of the item, even though the reference was to the MHRA Drug Safety Update publication and not the MHRA *per se*.

2 Use of the word 'new'

Avamys received its marketing authorization in January 2008. However, it was not available in the UK because GlaxoSmithKline did not market or distribute it until late 2008. Avamys was launched in the UK in February 2009, representatives were trained in the second half of January 2009 and the product was launched to the medical press on 9 February 2009. Due to the availability of the product licence, representatives were able to promote the product from the start of February 2009.

GlaxoSmithKline provided a copy of the current detail aid for Avamys, which was used from April 2010 and did not use the word 'new'.

In the spirit of transparency GlaxoSmithKline included information which outlined the communications associated with the launch of Avamys and the withdrawal of materials used in the first year that Avamys was marketed in the UK. All promotional staff were emailed on 4 February 2010 and asked to immediately stop using their current materials and return them for destruction. Replacement materials that did not use the word 'new' were provided later that week (Avamys detail aid dated January 2010). GlaxoSmithKline believed that the action it had taken resulted in continued compliance with Clause 7.11, which required that 'new' must not be used to describe any product that had been generally available for more than 12 months.

Due to the documented actions taken and materials provided, in which 'new' was not used, GlaxoSmithKline did not believe that it was in breach of Clause 7.11.

In response to a request for further information

GlaxoSmithKline stated that Avamys was launched internally, to representatives, on Thursday, 29 January 2009 after the product training, which took place earlier that week. That was why Avamys was referred to as having reached its first birthday on 29 January 2010 in the 'Recall of Avamys Campaign Materials' letter sent with the initial response.

Promotion could start Friday, 30 January when the representatives returned to their regions after the training meeting, with the majority of relevant representatives fully engaged in Avamys promotional activities on Monday 2 February 2009. The press release was issued on Monday 9 February 2009.

Promotional activities were mainly directed at GPs and pharmacists.

3 Prescribing information on health professional websites

GlaxoSmithKline was unsure as to which specific websites were being referred to. However, it provided copies of screen shots of its health professional website (http://hcp.gsk.co.uk/) for Seretide, Avamys and Rupafin. This website provided information based on the summary of product characteristics (SPC) on all its products including links to the SPC, patient information leaflet and the prescribing information for all medicines promoted by GlaxoSmithKline. GlaxoSmithKline provided copies of the relevant initial web pages and the prescribing information pages and noted the clear link to the relevant prescribing information. GlaxoSmithKline therefore denied a breach of Clause 4.1.

4 Training of medical representatives and targets for Rupafin

GlaxoSmithKline viewed the training of all staff involved with any medicine as critical to the success of the medicine and to relationships it had with its customers and the care they offered to their patients. This included clear and comprehensive training of relevant staff such that health professionals could be informed about the appropriate use of GlaxoSmithKline medicines in relevant patients. The Rupafin (rupatadine) training was composed of the following:

- Distance learning using a training manual with support and assessment of knowledge by field trainers.
- Regional road shows – one day workshops in all regions to consolidate distance learning (September 2009). This included a examination.
- Rolling diary of 5 day training, week starting 28 September 2009 for Rupafin and Avamys, as both products would be detailed by the same representatives – intended for new representatives and those that required refresher training.
- Post regional road show evaluation to assess level of satisfaction with the content and format of the regional conference.

As part of this comprehensive training plan, the targets for the brand and individuals were discussed. The targets were discussed down to an individual level, with opportunity for challenge if required. Given the market for anti-histamines and the way GlaxoSmithKline intended to position Rupafin, GlaxoSmithKline believed that the targets were ambitious but achievable and did not create any incentives that were counter to maintaining the highest ethical standards, which GlaxoSmithKline believed its representatives operated to at all times.

In response to a request for further information GlaxoSmithKline provided selected slides from the regional Rupafin road show training session for representatives one of which presented the Rupafin targets for 2009-2013 (targets had been revised for 2010-2013 this year). Another slide showed the Rupafin sales target for the final quarter of 2009. A third slide detailed the weighting of a representative's short term reward from Rupafin sales.

GlaxoSmithKline submitted that the targets set for the sales team and for individuals were not unrealistic or excessive or likely to encourage unethical behaviour. Irrespective of the targets set for any medicine, GlaxoSmithKline continued to believe its representatives operated to high ethical standards.

GlaxoSmithKline submitted that the documents provided demonstrated that the training plan was comprehensive, well planned and well monitored. This included the clear communication of the relevant therapy area, medicine and sales technique information as well as assessment and seeking of opinion of the representatives that had been trained. This was in addition to the annual Code training and GlaxoSmithKline's culture of ethical compliance that was in place for all promotional representatives.

GlaxoSmithKline remained committed to encouraging a culture of quality and compliance within the company. It trusted the Authority would agree that it had maintained the highest ethical standards in all activities carried out by the respiratory and allergy team. GlaxoSmithKline therefore believed that it was not in breach of Clauses 4.1, 7.11, 9.5, 15.2, 15.4, 15.9, 16.1 and 9.1.

GlaxoSmithKline again queried whether this complaint should proceed at all given the lack of evidence to support the anonymous medical contractor's serious allegations.

PANEL RULING

The Panel noted GlaxoSmithKline's concerns about the lack of evidence from the anonymous complainant. Nevertheless, a complaint had been made from which it appeared that a company might have breached the Code and, as set out in Paragraph 5.1 of the Constitution and Procedure, it needed to be considered bearing in mind that the

complainant had the burden of proving their complaint on the balance of probabilities.

1 References to the MHRA

The Panel noted that a Seretide leavepiece included the claim 'To aid compliance with the concomitant use of ICS [inhaled corticosteroid] and LABA, a combination inhaler should be used when appropriate (MHRA Drug Safety Update)[4]'. Reference 4 given on the last page also included mention of the MHRA.

The Seretide detail aid included the claim 'To aid compliance with the concomitant use of inhaled corticosteroids and LABA, a combination inhaler should be used when appropriate[13]'. Reference 13 given on the last page included mention of the MHRA.

Clause 9.5 stated that promotional material must not include **any** (emphasis added) reference to, *inter alia*, the MHRA, unless this was specifically required by the MHRA. The Panel thus ruled that the detail aid and the leavepiece were each in breach of Clause 9.5. The Panel noted that the leavepiece had already been withdrawn because of the reference to the MHRA.

2 Use of word the word 'new'

The Panel noted that promotion of Avamys started on 2 February 2009. The email instructing representatives to stop using current materials, sent on 4 February 2010 at 18:29, referred to immediately recalling certain items that no longer complied with the Code. The email stated that the issue related to the use of the word 'new' that appeared on certain items. Material describing Avamys as new had not been recalled until after the close of business on 4 February 2010 and so in that regard it had been used for more than twelve months. Thus the Panel ruled a breach of Clause 7.11.

3 Prescribing information on health professional websites

The Panel noted that the complainant had not provided any detail or examples of where prescribing information had not been provided. The Panel noted that material provided by GlaxoSmithKline showed that prescribing information was provided as a link on the website pages. On the basis of the information before it, the Panel ruled no breach of Clause 4.1.

4 Training of medical representatives and targets for Rupafin

The Panel noted that detailed training was provided for representatives promoting Rupafin. No breach of Clause 16.1 was ruled.

With regard to targets for such representatives the Panel noted GlaxoSmithKline's submission that its targets were ambitious but achievable. The targets had been revised this year. The Panel noted that no information had been provided by the complainant about what was unrealistic about the targets nor about the alleged target driven, unethical practices by representatives. The Panel decided that on the basis of the information before it there was no breach of Clauses 15.2, 15.4, and 15.9 and ruled accordingly.

The Panel noted its rulings above and did not consider that overall GlaxoSmithKline had failed to maintain a high standard; no breach of Clause 9.1 was ruled.

Complaint received **27 July 2010**

Case completed **20 September 2010**

CASE AUTH/2337/7/10

MERCK SERONO v SANDOZ

Press release and article on Omnitrope

Merck Serono complained about a global press release about Omnitrope (somatropin) issued in Germany by Sandoz and about an article which had allegedly been published in a UK patient support group newsletter entitled 'Biosimilars, NICE [National Institute for Health and Clinical Excellence] and Omnitrope'. Merck Serono supplied Saizen (somatropin). Both products were growth hormones. Omnitrope was a biosimilar.

The detailed response from Sandoz is given below.

With regard to the sentence in the press release 'Latest NICE cost-benefit guidance includes Sandoz's Omnitrope as one of seven recommended somatropin products to treat growth failure in children', Merck Serono stated that NICE referred to cost and effectiveness but no cost-benefit guidance was issued.

In the Panel's view the press release was subject to the UK Code. Whilst issued by Sandoz's German headquarters it discussed the UK NICE guidance and referred to cost savings to the NHS. Sandoz was thus responsible for the press release under the Code.

The Panel noted that the relevant NICE guidance referred to the acquisition cost of various somatropins their clinical effectiveness and cost-effectiveness. The Panel considered that most readers would assume that the term 'cost-benefit' meant more than separate analyses of the product's acquisition costs and clinical effectiveness. Given the detailed discussion of somatropins' cost-effectiveness the Panel did not consider that the term 'cost-benefit' misled as to the content of the NICE guideline on this point. No breach of the Code was ruled.

With regard to the sentence 'Guidance recommends that, where more than one product is suitable, the least costly option should be chosen', Merck Serono alleged that the NICE guidance had been misquoted to imply that cost was the key consideration in choosing growth hormone.

The Panel did not consider that the press release was misleading on this point. It did not state or imply that cost was the key consideration as alleged. It was made clear that only where more than one product was suitable then the least costly should be chosen. No breach of the Code was ruled.

Merck Serono alleged that the phrase 'no differences' in the sentence 'The guidance issued by the NICE Appraisal Committee noted that Omnitrope had undertaken head-to-head trials with the reference product as part of its regulatory submission to the European Medicines Agency (EMA) and found that there were no differences in terms of safety or efficacy between the products' was misleading and unsubstantiated.

The Panel noted that the press release began by introducing the NICE guidance and stating that it recommended the use of Sandoz's product Omnitrope as one of seven recommended products. It was the first time NICE had recommended the use of a biosimilar. This was followed by the sentence at issue. The press release continued by stating that biosimilars were approved by the EMA on the basis that they had demonstrated comparable quality, safety and efficacy to their reference product.

The Panel noted that the licensing approval process for Omnitrope, as a biosimilar, was discussed in the NICE guidance which noted that in general terms the originator biopharmaceutical product could not be copied exactly and that this might lead to different immunological effects and that biosimilar products might have a different safety profile from the originator product. It was noted that EMEA legislation on biosimilars defined the studies needed to demonstrate equivalent safety and efficacy to the pharmaceutical reference product. It was also noted that making specific recommendations around the safety of a medicine was outside NICE's remit, that no evidence had been submitted on differences between the biosimilar (Omnitrope) and the originator product in terms of safety or efficacy, and that the current prescribing advice referred to prescription of biopharmaceutical products by brand name. Based on the marketing authorization for Omnitrope NICE was satisfied that it could be considered for the treatment of growth failure alongside the other six somatropin products.

In relation to clinical effectiveness the NICE guidance stated that 'there appeared to be no difference in the clinical effectiveness of the various somatropin products available'. It was further noted that the studies submitted to the EMEA '… provided evidence on the equivalence [Omnitrope and the originator product]'. It did not state 'evidence of equivalence' as submitted by Sandoz. The guidance did not state that the somatropin products showed no differences in relation to efficacy nor that there were no differences on safety. It was expressly stated that making recommendations about safety was beyond NICE's remit. The Panel considered that the claim at issue was not an accurate reflection of the comments in

the NICE guidance about the product's safety and efficacy. The claim at issue was misleading in this regard and a breach of the Code was ruled.

Merck Serono alleged that the original NICE guidance had been paraphrased / misquoted to imply that cost was the first and key consideration in choosing growth hormone. In this regard it referred to the sentence 'NICE says that, when more than one product is suitable, the least costly option should be chosen. NICE recommended that a discussion should be held between a clinician and patient to choose the somatropin treatment received, based on therapeutic need and the likelihood of adherence to treatment'.

The Panel considered its ruling above was relevant here. The Panel did not consider that the claim at issue was misleading as alleged. No breach of the Code was ruled.

Merck Serono referred to the quotation from a named consultant paediatrician that 'I have 10 years of clinical experience using Omnitrope with my paediatric patients and I believe it is both effective and well tolerated. I welcome the decision by NICE to recommend the option of a biosimilar; it will benefit patients by providing an alternative, equally effective treatment option as well as offering much needed cost savings to the NHS'. Merck Serono alleged that the quotation that Omnitrope was an 'equally effective treatment option' was misleading. Merck Serono was also concerned that this quotation referred to the paediatrician's 10 years of clinical experience with Omnitrope. This was unsubstantiated as was the reference to Omnitrope being able to 'offer much needed cost savings to the NHS'.

The Panel noted the submission that the quotation was the clinical opinion of a named paediatrician. The Panel noted that this was a company press release which it had decided was covered by the Code and thus its entire content must comply with the Code irrespective of whether any part of it represented the personal view of a clinician.

Merck Serono had alleged that the phrase 'an equally effective treatment option' was misleading but had not provided reasons. Other allegations above related to whether the descriptions in the press release fairly reflected the NICE guidance. It was not entirely clear whether the named doctor was referring to the concept of recommending a biosimilar in order to benefit patients by providing an alternative, equally effective treatment option and offer much needed cost savings to the NHS or attributing these qualities specifically to Omnitrope. The Panel noted its ruling above which had related to a slightly different point, namely whether the press release fairly reflected the NICE guidance in relation to the claim that there were 'no differences in terms of safety or efficacy between the products.' The Panel considered that if the phrase 'an equally effective treatment option' related to biosimilars as a class it was not necessarily a misleading description of a biosimilar. No comparative efficacy evidence had been submitted by either party in relation to Omnitrope and its reference product. The Panel noted that the complainant, Merck Serono, had to establish its case on the balance of probabilities. No breach of the Code was ruled.

The Panel noted Sandoz's submission that the named doctor had been involved in the early stage development of Omnitrope. The Panel did not consider that the phrase '10 years of clinical experience' was misleading as alleged. No breach of the Code was ruled.

The Panel noted that at the time of publication the price of Omnitrope had been reduced making it the least expensive growth hormone in the UK on list price. Sandoz also referred to clear positive, cost-benefits compared to other somatropin preparations. The Panel noted that the claim at issue was very general and simply referred to cost savings to the NHS, it did not state or imply that the cost savings would be greater than with all other somatropins. No breach of the Code was ruled.

Merck Serono alleged that the reference to Omnitrope in a patient newsletter clearly breached the Code. Merck Serono was also aware that this was sent to the patient group unsolicited.

Merck Serono alleged that the statement '…the NICE panel deemed it to be as safe and effective as the other Somatropin products …' implied that Omnitrope offered the same efficacy and safety as other somatropins. NICE guidance did not state that Omnitrope offered the same efficacy and safety as other somatropins.

Merck Serono alleged that the statement that 'Omnitrope is 26% less expensive than the most widely prescribed product in the UK' was unsubstantiated as was the statement 'Omnitrope … offers clear savings without compromising patient care or support'.

It was unclear whether the article had been written solely by the named consultant paediatrician or whether Sandoz was involved in the development of its content. There did not appear to be any declaration of the involvement of Sandoz in the production of this article.

Merck Serono further alleged that the combination of advertising medicines to the public, providing misleading information, claims and comparisons and not declaring sponsorship constituted a breach of Clause 2.

The Panel noted that the article at issue had not been published in the patient group newsletter or otherwise used by the company. A version which was clearly a draft had been distributed for comment. Given that the item was not in its final

form and had not been used as described above the Panel ruled no breach of the Code including Clause 2.

Merck Serono complained about a press release about Omnitrope (somatropin) issued by Sandoz and about an article which had allegedly been published in a patient support group newsletter entitled 'Biosimilars, NICE [National Institute for Health and Clinical Excellence] and Omnitrope'. Inter-company dialogue had failed to resolve the matter. Merck Serono supplied Saizen (somatropin). Both products were growth hormones. Omnitrope was a biosimilar.

A Press release

Sandoz explained that the item was a global press release, issued by its head office in Germany, as was apparent from the press release. The press release was not certified but it was examined to ensure that it did not breach the Code or relevant statutory requirements. When Merck Serono raised its initial concerns on 14 June it was advised that this was a global press release and that it should discuss the matter with Sandoz's global headquarters. Merck insisted on dealing locally and so, to show good will and aid inter-company dialogue, Sandoz agreed to discuss the matter.

1 Claim 'Latest NICE cost-benefit guidance includes Sandoz's Omnitrope as one of seven recommended somatropin products to treat growth failure in children'

COMPLAINT

Merck Serono stated that the NICE referred to cost and effectiveness but no cost-benefit guidance was issued. A breach of Clause 7.2 was alleged.

RESPONSE

Sandoz stated that the press release did not quote the NICE guidance document directly. Sandoz's interpretation of cost-benefit and cost-effectiveness was that the two terms had the same inference.

The NICE website listed the following point as one of the definitions of what NICE guidance was:

'Good value for money, weighing up the cost and benefits of treatments'

Section 4.2 'Cost effectiveness' of the NICE guidance [Human growth hormone (somatropin) for the treatment of growth failure in children] clearly included a detailed assessment of the cost-effectiveness of somatropin. Furthermore the guidance increased the access to patients through two newly approved indications, small for gestational age (SGA) and short stature homeobox-containing gene (SHOX) deficiency, based on cost vs patient benefit. Sandoz therefore did not see why the use of the term 'Latest NICE cost-benefit guidance' would be misleading.

PANEL RULING

The Panel noted Sandoz's general comments about the international nature of the press release and was concerned that it appeared only to have agreed to discuss Merck Serono's concerns on a local UK level merely to show good will. In the Panel's view the press release was subject to the UK Code. Whilst issued by Sandoz's German headquarters it discussed the UK NICE guidance and referred to cost savings to the NHS. Sandoz was thus responsible for the press release under the Code and obliged to enter into inter-company dialogue at a UK level.

The Panel noted that the relevant NICE guidance not only referred to the acquisition cost of various somatropins (Section 3.5) but also discussed their clinical effectiveness (Section 4.1) and cost-effectiveness (Section 4.2). The Panel considered that most readers would assume that the term 'cost-benefit' meant more than separate analyses of the product's acquisition costs and clinical effectiveness. Given the detailed discussion of somatropins' cost-effectiveness the Panel did not consider that the term 'cost-benefit' misled as to the content of the NICE guideline on this point. No breach of Clause 7.2 was ruled.

2 Claim 'Guidance recommends that, where more than one product is suitable, the least costly option should be chosen'

COMPLAINT

Merck Serono alleged that the NICE guidance had been misquoted to imply that cost was the key consideration in choosing growth hormone. A breach of Clause 7.2 was alleged.

RESPONSE

Sandoz noted that the press release did not state that the guidance recommended that the least costly option should be chosen. It expressly contained a pre-condition for such choice by stating that, '**where** more than one product **is suitable**, the least costly option should be chosen' (emphasis added). It was in the nature of such a pre-condition that it must be fulfilled before cost was taken into account. The press release also gave a detailed explanation of the term 'suitable' by stating that 'NICE recommended that a discussion should be held between a clinician and patient to choose the somatropin treatment received, based on therapeutic need and the likelihood of adherence to treatment'.

It stated that the least costly option should be chosen where more than one product was suitable, implying it was still an important factor.

PANEL RULING

The Panel did not consider that the press release was misleading on this point. It did not state or

imply that cost was the key consideration as alleged. It was made clear that only where more than one product was suitable then the least costly should be chosen. No breach of Clause 7.2 was ruled.

3 Claim 'The guidance issued by the NICE Appraisal Committee noted that Omnitrope had undertaken head-to-head trials with the reference product as part of its regulatory submission to the European Medicines Agency (EMA) and found that there were no differences in terms of safety or efficacy between the products'

This claim was referenced to the NICE guidance and the Omnitrope European Public Assessment Report (EPAR).

COMPLAINT

Merck Serono alleged that the phrase 'no differences' was misleading and unsubstantiated in breach of Clause 7.2.

RESPONSE

Sandoz stated that Section 4.3.5 of the NICE guidance used the phrase 'evidence of equivalence'. The claim at issue was from the guidance, Section 4.3.5 stated that, 'The Committee agreed that there appeared to be no differences in the clinical effectiveness of the various somatropin products available'.

Therefore, Sandoz believed the claim at issue was substantiated.

PANEL RULING

The Panel noted that the press release began by introducing the NICE guidance and stating that it recommended the use of Sandoz's product Omnitrope as one of seven recommended products. It was the first time NICE had recommended the use of a biosimilar. This was followed by the sentence at issue. The press release continued by stating that biosimilars were approved by the EMA on the basis that they had demonstrated comparable quality, safety and efficacy to their reference product.

The Panel noted that the licensing approval process for Omnitrope, as a biosimilar, was discussed at Section 4.3.4 of the NICE guidance. The guidance noted that in general terms the originator biopharmaceutical product could not be copied exactly and that this might lead to different immunological effects and that biosimilar products might have a different safety profile from the originator product. It was noted that EMEA legislation on biosimilars defined the studies needed to demonstrate equivalent safety and efficacy to the pharmaceutical reference product. It was noted that making specific recommendations around the safety of a medicine was outside NICE's remit, that no evidence had been submitted on differences between the biosimilar (Omnitrope) and the originator product in terms of safety or efficacy, and that the current prescribing advice referred to prescription of biopharmaceutical products by brand name. Based on the marketing authorization for Omnitrope NICE was satisfied that it could be considered for the treatment of growth failure alongside the other six somatropin products.

In relation to clinical effectiveness, Section 4.3.5 of the NICE guidance stated that 'there **appeared to be** no difference in the clinical effectiveness of the various somatropin products available.' (emphasis added). It was further noted that the studies submitted to the EMEA '… provided evidence on the equivalence [Omnitrope and the originator product]'. It did not state 'evidence of equivalence' as submitted by Sandoz. Section 4.3.5 did not state that the somatropin products showed no differences in relation to efficacy nor that there were no differences on safety. Section 4.3.4 expressly stated that making recommendations about safety was beyond NICE's remit. The Panel considered that the claim at issue was not an accurate reflection of the comments in the NICE guidance about the product's safety and efficacy. The claim at issue was misleading in this regard and a breach of Clause 7.2 was ruled.

4 Claim 'NICE says that, when more than one product is suitable, the least costly option should be chosen. NICE recommended that a discussion should be held between a clinician and patient to choose the somatropin treatment received, based on therapeutic need and the likelihood of adherence to treatment'

COMPLAINT

Merck Serono alleged that the original NICE guidance had been paraphrased / misquoted to give the impression that cost was the first and key consideration in choosing growth hormone in breach of Clause 7.2.

RESPONSE

Sandoz stated that this point had already been addressed in response to point A2 above. Sandoz endeavoured to ensure that the press release was a fair representation of the guidance with respect to accuracy and content. As noted above, Sandoz consulted NICE before the piece was published.

PANEL RULING

The Panel considered its ruling at point A2 above was relevant here. The Panel did not consider that the claim at issue was misleading as alleged. No breach of Clause 7.2 was ruled.

5 Claim 'a named consultant paediatrician …said: "I have 10 years of clinical experience using

Omnitrope with my paediatric patients and I believe it is both effective and well tolerated. I welcome the decision by NICE to recommend the option of a biosimilar; it will benefit patients by providing an alternative, equally effective treatment option as well as offering much needed cost savings to the NHS."'

COMPLAINT

Merck Serono alleged that the reference to Omnitrope being an 'equally effective treatment option' was misleading. Merck Serono was also concerned that this quotation referred to the named paediatrician's 10 years of clinical experience with Omnitrope. This was unsubstantiated as was the reference to Omnitrope being able to 'offer much needed cost savings to the NHS'. A breach of Clause 7.2 was alleged.

RESPONSE

Sandoz stated that this was the named paediatrician's clinical opinion, which it supported. Furthermore, the consultant paediatrician was involved in the early stage development of Omnitrope, which began in 1998. He was involved in the first human trials, in February 2000, which gave him a unique standpoint on which to comment. He had not been briefed by Sandoz; this was his personal opinion having used the product for many years, and his in-depth understanding of biosimilars being involved in the trials. Sandoz therefore had no reason to believe that the consultant's opinion would be incorrect or misleading.

Section 4.3.5 of the NICE guidance supported the equivalence of the two products. The named consultant paediatrician was only supporting this claim in his statement.

With regard to the statement about much needed cost savings to the NHS, while this was a personal opinion, Sandoz added that from relative cost comparison per mg as in Section 3.5 of the NICE guidance, there were clear, positive, cost-benefits with use of Omnitrope compared with some of the other somatropin preparations. In addition, at the time of publication the price of Omnitrope had been further reduced making it the least expensive growth hormone in the UK on list price.

A copy of 'A Report Detailing the Economic Value of Omnitrope in England and Wales' was provided.

PANEL RULING

The Panel noted the submission that the quotation at issue was the clinical opinion a named consultant paediatrician which the company supported and that he had not been briefed by Sandoz. The Panel noted that this was a company press release which it had decided was covered by the Code and thus its entire content must comply with the Code irrespective of whether any part of it represented the personal view of a clinician.

Merck Serono had alleged that the phrase 'an equally effective treatment option' was misleading but had not provided reasons. Other allegations above related to whether the descriptions in the press release fairly reflected the NICE guidance. It was not entirely clear whether the consultant paediatrician was referring to the concept of recommending a biosimilar in order to benefit patients by providing an alternative, equally effective treatment option and offer much needed cost savings to the NHS or attributing these qualities specifically to Omnitrope. The Panel noted its ruling in point A3 which had related to a slightly different point, namely whether the press release fairly reflected the NICE guidance in relation to the claim that there were 'no differences in terms of safety or efficacy between the products.' The Panel considered that if the phrase 'an equally effective treatment option' related to biosimilars as a class it was not necessarily a misleading description of a biosimilar. No comparative efficacy evidence had been submitted by either party in relation to Omnitrope and its reference product. The Panel noted that the complainant, Merck Serono, had to establish its case on the balance of probabilities. No breach of Clause 7.2 was ruled.

The Panel noted Sandoz's submission that the consultant paediatrician had been involved in the early stage development of Omnitrope. The Panel did not consider that the phrase '10 years of clinical experience' was misleading as alleged. No breach of Clause 7.2 was ruled.

The Panel noted that at the time of publication the price of Omnitrope had been reduced making it the least expensive growth hormone in the UK on list price. Sandoz also referred to clear positive, cost-benefits compared with other somatropin preparations. The Panel noted that the claim at issue was very general and simply referred to cost savings to the NHS, it did not state or imply that the cost savings would be greater than with all other somatropins. No breach of Clause 7.2 was ruled.

B Article in patient support group newsletter 'Biosimilars, NICE and Omnitrope'

This article was attributed to the named consultant paediatrician.

COMPLAINT

Merck Serono alleged that the reference to Omnitrope in a patient newsletter clearly breached Clause 22.1. Merck Serono was also aware that this was sent to the patient group unsolicited.

Merck Serono alleged that the statement '…the NICE panel deemed it to be as safe and effective as the other Somatropin products …' implied that Omnitrope offered the same efficacy and safety as other somatropins. NICE did not issue any guidance that said that Omnitrope offered the same efficacy

and safety as other somatropins. Merck Serono alleged a breach of Clause 7.2.

Merck Serono alleged that the statement that 'Omnitrope is 26% less expensive than the most widely prescribed product in the UK' was unsubstantiated in breach of Clause 7.2 as was the statement 'Omnitrope … offers clear savings without compromising patient care or support'.

It was unclear whether the article had been written solely by the named consultant paediatrician or whether Sandoz was involved in the development of its content. There did not appear to be any declaration of the involvement of Sandoz in the production of this article. Merck Serono alleged a breach of Clause 9.10.

Merck Serono further alleged that the combination of advertising medicines to the public, providing misleading information, claims and comparisons and not declaring sponsorship constituted a breach of Clause 2.

RESPONSE

Sandoz stated that it first met the chairman of the patient support group when he gave advice on behalf of the group at the NICE committee meeting reviewing its guidance document, 'Human growth hormone (somatropin) for the treatment of growth failure in children' and indicated that Sandoz was the only company that had never engaged with the patient group. At that time the chairman knew little about biosimilars and the patient group would not be in a position to recommend them to its members. Following these comments Sandoz and the patient group agreed to meet and discuss the principles behind biosimilars.

The patient group chairman, the consultant paediatrician (invited by the chairman) and Sandoz met on 2 June 2010 and following a short discussion about biosimilars, the chairman decided it would be applicable for the consultant paediatrician to clarify some of the misconceptions surrounding them and write a piece for the patient group newsletter. Therefore this piece was not solicited by Sandoz.

Before the consultant's piece was published, the patient group distributed the article (as a word document and not in its final form) to all other growth hormone suppliers to ensure that it was not a biased or unfair representation. A copy was provided. The other companies were able to comment on the proposed article. The consultant paediatrician had added a Sandoz employee to the authors list as he was present at the original meeting. Sandoz was not fully aware of this. To reiterate, when the consultant's article was sent out for comment it was not approved in its final form and had not been published.

As soon as Sandoz realised that this could breach the Code, it informed the consultant that the piece should be withdrawn immediately to avoid any risk that it would be seen as disguised promotion. This was before the item went through the certification procedure. The consultant informed the patient group and the article was withdrawn. The article was not published and Sandoz did not intend to publish it in the future. A copy of an email of 7 July 2010 from the patient group confirming that the consultant had requested the proposed article to be withdrawn was provided.

Sandoz did not consider that it had breached the Code as this material had never been publicly available.

PANEL RULING

The Panel noted that the article at issue had not been published in the patient group newsletter or otherwise used by the company. A version which was clearly a draft had been distributed for comment. Given that the item was not in its final form and had not been used as described above the Panel ruled no breach of Clauses 2, 7.2, 9.10 and 22.1 of the Code.

Complaint received **28 July 2010**

Case completed **25 October 2010**

CASE AUTH/2338/7/10

ESPRIT v DEXCEL PHARMA

Deximune mailing

ESPRIT (Efficacy and Safety of Prescribing in Transplantation) alleged that a one page, A4 mailing for Deximune (ciclosporin) sent by Dexcel Pharma, headed 'Ciclosporin Prescribing in the UK The Facts', had the potential to negatively impact patient safety.

ESPRIT noted that official UK recommendations clearly stated if it was necessary to switch a patient stabilised on one brand of ciclosporin to another brand, the patient should be monitored closely for side-effects, blood-ciclosporin concentration and transplant function.

ESPRIT supported these recommendations which were in line with its own recommendations. Unfortunately the mailing at issue, particularly the assertion that patients could be switched without the need for dose adjustment, with no stipulation for monitoring, was at odds with such recommendations, which were made in the interest of patient safety. Indeed, ESPRIT believed it was contrary to the provisions of the Deximune summary of product characteristics (SPC).

The detailed response from Dexcel Pharma is given below.

The Panel noted that the mailing at issue featured a number of claims in bold, bright blue font. One of these was 'There is no significant difference between the absorption of ciclosporin from Deximune and Neoral under fed and fasted conditions'. This was immediately followed, in plain, black type by the next paragraph which began 'Because of the differences in absorption between fed and fasted conditions with previous formulations of ciclosporin the current recommendations are for close monitoring when switching any formulation of ciclosporin.' This was, in turn, followed by another claim in bold, bright blue font that 'However, patients can be started on Deximune or switched to Deximune from Neoral without the need for dose adjustment'.

The Deximune SPC stated the following:

'Due to differences in bioavailability between different oral formulations of ciclosporin it is important that health professionals and patients be aware that substitution of Deximune Capsules for other formulations may lead to alterations in ciclosporin blood levels.

Therefore patients should not be transferred to or from other oral formulations of ciclosporin without appropriate close monitoring of ciclosporin blood concentrations, serum creatinine levels and blood pressure.'

The Panel noted the presentation and layout of the mailing and considered that the reader's eye would be drawn to the claims in bright blue text such that they were likely to overlook the statement inbetween about the current recommendations for close monitoring. In the Panel's view, however, the statement regarding monitoring was, in any case, insufficient in that the Deximune SPC specifically referred to the close monitoring of ciclosporin blood concentrations, serum creatinine levels and blood pressure. The Panel noted that although the mailing had been used with hospital consultants, it had also been used widely with non-specialist health professionals. In the Panel's view, although some of the target audience would be experienced and knowledgeable about the use of ciclosporins, and thus familiar with content of the SPCs with regard to switching, others would not and so detailed knowledge in that regard should not be assumed. Overall, the Panel considered that the mailing was misleading with regard to the precautions necessary when switching a patient from Neoral to Deximune. A breach of the Code was ruled. The Panel considered that the claims were not consistent with the particulars listed in the Deximune SPC. A breach of the Code was ruled.

The Panel noted its comments above and considered that the mailing had the potential to adversely affect patient safety. Although there were no reports before the Panel to suggest that patient care had been adversely affected, it nonetheless considered that high standards had not been maintained. A breach of the Code was ruled.

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

ESPRIT (Efficacy and Safety of Prescribing in Transplantation) complained about a one page, A4 mailing for Deximune (ciclosporin) sent by Dexcel Pharma Limited. The mailing was headed 'Ciclosporin Prescribing in the UK The Facts'.

COMPLAINT

ESPRIT was concerned that the mailing at issue had a real potential to negatively impact patient safety and in that regard noted that official recommendations regarding use of different formulations of ciclosporin were clear, as exemplified by the following:

> 'Patients should be stabilised on a single brand of oral ciclosporin because switching between

formulations without close monitoring may lead to clinically important changes in bioavailability. Prescribing and dispensing of ciclosporin should be by brand name to avoid inadvertent switching. If it is necessary to switch a patient stabilised on one brand of ciclosporin to another brand, the patient should be monitored closely for side-effects, blood-ciclosporin concentration, and transplant function.' (ref current British National Formulary (BNF)).

and

'Patients should be stabilised on a single brand of ciclosporin because switching between formulations without monitoring may lead to clinically important changes in bioavailability. All products that contain ciclosporin are interchangeable **only** if careful therapeutic monitoring takes place. Prescribing and dispensing of ciclosporin should be by brand name to avoid inadvertent switching.' (ref Medicines and Healthcare products Regulatory Agency (MHRA) Drug Safety Update, December 2009)

ESPRIT fully supported these recommendations. Indeed, they were wholly in line with its own recommendations made following an in-depth examination of available data. Unfortunately, the mailing at issue, particularly the assertion that patients could be switched without the need for dose adjustment, with no stipulation for monitoring, was at odds with such recommendations, which were made in the interest of patient safety. Indeed, ESPRIT believed it was contrary to the provisions of the Deximune summary of product characteristics (SPC).

When writing to Dexcel Pharma, the Authority asked it to respond in relation to Clauses 2, 3.2, 7.2 and 9.1 of the Code.

RESPONSE

Dexcel submitted that Deximune had been demonstrated to be bioequivalent to Neoral. This was confirmed by healthy volunteer studies under fed and fasting conditions. The data from these studies was included in the Deximune SPC. In addition, a post-marketing, retrospective, parallel, multicenter survey in transplant patients receiving these two formulations compared their toxicity profiles and bioavailability (Berger *et al* 2008). Of the patients reviewed, 157 out of 174 received both products; Neoral was administered first and then the patients were transferred to Deximune. Ciclosporin blood levels measurements were taken on three occasions during the review period. The results confirmed the bioequivalence of the two products in this patient population using analytical programs which took account of the patient variables. In addition, the products were deemed to have similar toxicity profiles and as a result the investigators concluded that the two products could be interchanged without the need for dosage adjustment while monitoring blood levels, blood pressure and renal function, all of which were recorded in the study.

UK patients were last switched from one formulation of ciclosporin to another when Neoral was introduced; over a period of time the majority of patients were switched from Sandimmune to Neoral. Dexcel understood from prescribers that patients were switched on a dose for dose basis which resulted in changes in trough ciclosporin levels and rejection episodes for a number of patients. As a result, a significant number of prescribers had been concerned about the appropriate dose to start patients on Deximune, either *de-novo* or when switching from Neoral.

In the light of the bioequivalence information outlined above and the concern about the appropriate starting and switching dose for Deximune, this was an important issue that needed to be addressed. It was important from a safety point of view therefore to highlight the fact that when starting new patients on Deximune or when transferring patients from Neoral to Deximune, the dose should be the same as for Neoral. For this reason, the claim 'However patients can be started on Deximune or switched to Deximune from Neoral without the need for dose adjustment' was highlighted in the mailing to minimise the risk that a patient might be transferred on a higher or lower dose and so potentially be at risk of rejection or toxicity.

ESPRIT had claimed that Dexcel made no stipulation for monitoring, which was not so; the mailing clearly stated 'Because of the differences in absorption between fed and fasted patients with previous formulations of ciclosporin, the current recommendations are for close monitoring when switching any formulation of ciclosporin'. This claim immediately preceded the one regarding the starting dose which Dexcel considered was the appropriate positioning from a patient safety point of view. Dexcel had never, either verbally or in writing, suggested that Neoral patients should be switched to Deximune without close monitoring to confirm ciclosporin blood levels, renal function and blood pressure.

In December 2009 at the request of the MHRA, Dexcel sent a 'Dear Healthcare Professional' letter to 54,364 health professionals including: GPs; retail and hospital pharmacists; hospital doctors (from staff grade to professor) within dermatology, nephrology, paediatric nephrology, renal, rheumatology and transplant and pharmaceutical advisors in primary care trusts. This letter was approved by the MHRA and could be viewed on its website. The letter clearly highlighted the need to prescribe ciclosporin by brand, for close monitoring to be carried out when switching and that transplant patients should not have their brand of ciclosporin changed without the permission of the prescriber. This was the only communication that Dexcel had had with the majority of these health professionals.

By contrast, the mailing at issue was sent only to hospital consultants in renal medicine, transplantation and dermatology; hospital pharmacists; pharmaceutical advisors and medicines management pharmacists within primary care trusts; a total of 3,890 health professionals. The mailing had also been used subsequently at the British Renal Association/Renal Society joint meeting in May, The British Association of Dermatology meeting in July and in discussions with professionals who fell within the above groups. It would be reasonable to assume that these professionals were well informed on the need for close monitoring when prescribing ciclosporin for patients, particularly when switching between brands. However, as noted above, Dexcel considered it appropriate to remind them of the need for close monitoring when switching between brands. In addition, at no time after the mailing was sent or in subsequent 1:1 conversations, had any health professional complained to Dexcel about the content of the mailing. Furthermore, in the 10 months that Deximune had been available in the UK, Dexcel had had no reports of an adverse reaction as a result of a patient being switched from Neoral to Deximune.

Dexcel understood ESPRIT's concerns about ciclosporin prescribing. The group had worked closely with another pharmaceutical company over the last ten years to develop a consensus statement on ciclosporin based on experience of a number of generic formulations of ciclosporin that had been available in countries other than the UK. Their conclusions had shaped the current UK guidelines and recommendations.

Dexcel acknowledged that ESPRIT was now an independent organisation, and it had been keen to support its activities. In doing so Dexcel intended to ensure that it promoted Deximune in a responsible way and where appropriate, provided support to prescribers and patients when the ciclosporin of choice was Deximune. Notwithstanding that, Dexcel also needed to provide prescribers and potential prescribers with appropriate information for them to make an informed choice about which ciclosporin product to use. Decisions about ciclosporin prescribing were in the main made by hospital consultants, hospital pharmacists, primary care medicines management pharmacists and senior managers at hospital and PCT level. As a result, Dexcel's promotional activity had been mainly directed at these individuals.

In Dexcel's promotion of Deximune it had looked to convince the decision makers to arrive at an informed choice based on the clinical evidence and the cost effectiveness for Deximune. Dexcel had always taken into account patient safety and had never promoted Deximune outside of the scope of the SPC.

Dexcel submitted that it always aimed to work to the highest standards when producing its promotional materials and believed that the mailing at issue was no exception. Whilst highlighting the appropriate dose at which Deximune should be started for either new or switch patients, Dexcel had also included the current recommendations about close monitoring. In addition, in view of the fact that Dexcel had communicated with a well informed audience this further strengthened the point that patients had not been put at risk. Dexcel denied any breach of the Code.

PANEL RULING

The Panel noted that the mailing at issue featured a number of claims in bold, bright blue font. One of these was 'There is no significant difference between the absorption of ciclosporin from Deximune and Neoral under fed and fasted conditions'. This was immediately followed, in plain, black type by the next paragraph which began 'Because of the differences in absorption between fed and fasted conditions with previous formulations of ciclosporin the current recommendations are for close monitoring when switching any formulation of ciclosporin.' This was, in turn, followed by another claim in bold, bright blue font that 'However, patients can be started on Deximune or switched to Deximune from Neoral without the need for dose adjustment'.

The Deximune SPC stated the following:

> 'Due to differences in bioavailability between different oral formulations of ciclosporin it is important that health professionals and patients be aware that substitution of Deximune Capsules for other formulations may lead to alterations in ciclosporin blood levels.
>
> Therefore patients should not be transferred to or from other oral formulations of ciclosporin without appropriate close monitoring of ciclosporin blood concentrations, serum creatinine levels and blood pressure.'

The Panel noted the presentation and layout of the mailing and considered that the reader's eye would be drawn to the claims in bright blue text such that they were likely to overlook the statement inbetween about the current recommendations for close monitoring. In the Panel's view, however, the statement regarding monitoring was, in any case, insufficient in that the Deximune SPC specifically referred to the close monitoring of ciclosporin blood concentrations, serum creatinine levels and blood pressure. The Panel noted that although the mailing had been used with hospital consultants, it had also been used widely with non-specialist health professionals. In the Panel's view, although some of the target audience would be experienced and knowledgeable about the use of ciclosporins, and thus familiar with content of the SPCs with regard to switching, others would not and so detailed knowledge in that regard should not be assumed. Overall, the Panel considered that the mailing was

misleading with regard to the precautions necessary when switching a patient from Neoral to Deximune. A breach of Clause 7.2 was ruled. The Panel considered that the claims were not consistent with the particulars listed in the Deximune SPC. A breach of Clause 3.2 was ruled.

The Panel noted its comments above and considered that the mailing had the potential to adversely affect patient safety. Although there were no reports before the Panel to suggest that patient care had been adversely affected, it nonetheless considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

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

Complaint received **28 July 2010**

Case completed **10 September 2010**

CASE AUTH/2340/7/10

NOVARTIS v DEXCEL PHARMA

Promotion of Deximune

Novartis complained that a mailing and a detail aid for Deximune (ciclosporin), issued by Dexcel Pharma, failed to alert readers to the close monitoring that was required if patients stabilised on one brand of ciclosporin had to be switched to another. Novartis supplied Neoral (ciclosporin).

The detailed response from Dexcel Pharma is given below.

Novartis noted that recently updated UK guidance with regard to the switching of ciclosporin stated if it was necessary to switch a patient stabilised on one brand of ciclosporin to another brand, the patient should be closely monitored for side-effects, blood-ciclosporin concentration, and transplant function. Further, both the Deximune and Neoral summaries of product characteristics (SPCs) stated that patients should not be transferred to or from other oral formulations of ciclosporin without appropriate close monitoring of ciclosporin blood concentrations, serum creatinine and blood pressure.

Novartis noted that the mailing, 'Ciclosporin Prescribing in the UK The Facts', was available at the Dexcel stand at the British Transplant Society Annual Conference in March and was sent to the wider transplantation community including pharmacists. The claim at issue read 'Because of differences in absorption between fed and fasted conditions with previous formulations of ciclosporin the current recommendations are for close monitoring when switching any formulation of ciclosporin. *However, patients can be started on Deximune from Neoral without the need for dose adjustment.'* Noting the statement above from the Deximune SPC, Novartis submitted that use of the word 'however' and visual emphasis to the last sentence of the claim gave greater weight to the claim that no dose adjustment was required. Although this claim was true the visual emphasis to the final sentence allowed for ambiguity regarding the licensed requirement for close clinical monitoring of ciclosporin blood concentrations, serum creatinine levels and blood pressure, as stated in the Deximune SPC. Novartis alleged that this promotion was outside the terms of the marketing authorization.

Additionally, Novartis considered dose adjustments were a derivative of blood level monitoring and blood level monitoring to be a requirement of the terms of the marketing authorization. To claim that no dose adjustments were required when switching and visually emphasising this claim, created the perception that close blood level monitoring was not necessary or less important and thus misled the reader by implication and put the patient at risk of an inadvertent switch. Novartis noted that failure to closely monitor patients could lead to potential toxicity or underdosing with serious clinical implications including graft loss or death.

The Panel noted that in a closely similar complaint, Case AUTH/2338/7/10, it had noted that the mailing at issue featured a number of claims in bold, bright blue font. One of these was 'There is no significant difference between the absorption of ciclosporin from Deximune and Neoral under fed and fasted conditions'. This was immediately followed, in plain, black type by the next paragraph which began 'Because of the differences in absorption between fed and fasted conditions with the previous formulations of ciclosporin the current recommendations are for close monitoring when switching any formulation of ciclosporin'. This was, in turn, followed by another claim in bold, bright blue font that 'However, patients can be started on Deximune or switched to Deximune from Neoral without the need for dose adjustment'.

The Panel noted the presentation and layout of the mailing and considered that the reader's eye would be drawn to the claims in bright blue text such that they were likely to overlook the statement inbetween about the current recommendations for close monitoring. In the Panel's view, however, the statement regarding monitoring was, in any case, insufficient in that the Deximune SPC specifically referred to the close monitoring of ciclosporin blood concentrations, serum creatinine levels and blood pressure. The Panel noted that although the mailing had been used with hospital consultants, it had also been used widely with non-specialist health professionals. In the Panel's view, although some of the target audience would be experienced and knowledgeable about the use of ciclosporins, and thus familiar with content of the SPCs with regard to switching, others would not and so detailed knowledge in that regard should not be assumed. Overall, the Panel considered that the mailing was misleading with regard to the precautions necessary when switching a patient from Neoral to Deximune. A breach of the Code was ruled. The Panel considered that the claims were not consistent with the particulars listed in the Deximune SPC. A breach of the Code was ruled.

The Panel considered that its comments and rulings above in Case AUTH/2338/7/10 applied here in Case AUTH/2340/7/10. Breaches of the Code were ruled.

Novartis noted the claim on page 5 of the detail aid

that Deximune had been proved to: 'Be interchangeable with Neoral without the need for dose adjustment'. Nowhere in the detail aid were readers advised about the close monitoring of ciclosporin levels, serum creatinine and blood pressure which was required when switching between different formulations of ciclosporin.

Novartis submitted that claiming that no dose adjustments were required when switching, and by not providing any additional text to inform the reader of the need for close monitoring misled the reader and implied that close monitoring when switching patients was not necessary; this put the patient at risk of serious clinical implications. Novartis felt very strongly that the claims were inconsistent with the marketing authorization either by omission or through undue emphasis and implication.

The Panel noted that page 5 of the detail aid featured a number of bullet points about Deximune one of which stated that it had been proven to: 'Be interchangeable with Neoral without the need for dose adjustment'. The preceding bullet point stated that it had been proven to: 'Be equivalent to the innovator product, Neoral, under fed and fasted conditions'. There was no statement anywhere in the detail aid that if patients were switched from one brand of ciclosporin to another, close monitoring of ciclosporin blood concentrations, serum creatinine and blood pressure were required.

The Panel noted that the detail aid was available on-line for access by health professionals only. The Panel considered that a very wide audience might access the detail aid including those with little or no detailed knowledge of ciclosporin use. The Panel considered that the detail aid was misleading in its omission of detailed information about switching and not consistent with the Deximune SPC. Breaches of the Code were ruled. The Panel noted that Dexcel had not contested the complaint.

Novartis Pharmaceuticals UK Ltd complained about the promotion of Deximune (ciclosporin) by Dexcel Pharma Limited. At issue were a mailing (ref DEX/10/0013) and a detail aid (ref DEX/10/0001). Novartis supplied Neoral (ciclosporin). Inter-company dialogue had failed to resolve the matter.

By way of background Novartis noted that the recently updated guidance in the British National Formulary (BNF) with regard to the switching of ciclosporin stated:

> 'Patients should be stabilised on a single brand of oral ciclosporin because switching between formulations without close monitoring may lead to clinically important changes in bioavailability. Prescribing and dispensing of ciclosporin should be by brand name to avoid inadvertent switching. If it is necessary to switch a patient stabilised on one brand of ciclosporin to another brand, the patient should be closely monitored for side-effects, blood-ciclosporin concentration, and transplant function.'

Similarly, the December 2009 edition of the Drug Safety Update from the Medicines and Healthcare products Regulatory Agency (MHRA) stated:

> 'All products that contain ciclosporin should be prescribed by brand name to minimise the risk of inadvertent switching between brands, and to reflect advice in the British National Formulary.'

Novartis submitted that both the Deximune and Neoral summaries of product characteristics (SPCs) stated:

> 'Due to differences in bioavailability between different oral formulations of ciclosporin it is important that health professionals and patients be aware that substitution of [Deximune Capsules/Neoral] for other formulations may lead to alterations in ciclosporin blood levels. Therefore patients should not be transferred to or from other oral formulations of ciclosporin without appropriate close monitoring of ciclosporin blood concentrations, serum creatinine and blood pressure.'

A failure to remind of this requirement to carry out appropriate close monitoring was the basis of Novartis' complaint.

Novartis considered the materials at issue were not only in breach of the Code but also put patients at risk of harm; this was not a responsible way to promote a medicine in a complex therapeutic area. The potential cost of patient harm as a result of an uncontrolled inadvertent switch could be very high. Ciclosporin was routinely used not only in kidney but also heart and liver transplant, and in these patients acute rejection or toxicity could be fatal.

1 Mailing 'Ciclosporin Prescribing in the UK The Facts' (ref DEX/10/0013)

This mailing was available at the Dexcel stand at the British Transplant Society Annual Conference in March and, Novartis also believed, was sent to the wider transplantation community including pharmacists. The claim at issue read:

'Because of differences in absorption between fed and fasted conditions with previous formulations of ciclosporin the current recommendations are for close monitoring when switching any formulation of ciclosporin. **However, patients can be started on Deximune from Neoral without the need for dose adjustment.'**

COMPLAINT

Novartis noted the statement from the Deximune SPC above. The Code required any claim to be in accordance with the terms of the marketing authorization and to be accurate, objective, unambiguous and not to mislead either directly or

by implication or by undue emphasis.

Novartis submitted that use of the word 'however' and an emboldened typeface gave greater weight to the claim that no dose adjustment was required. Although this claim was true the bold type and implied extra weight to the final sentence allowed for ambiguity regarding the licensed requirement for close clinical monitoring of ciclosporin blood concentrations, serum creatinine levels and blood pressure, as stated in Section 4.2 of the Deximune SPC. Novartis considered that by allowing ambiguity in the interpretation of this paragraph through the bold text of the last sentence, the reader would question the requirement for therapeutic drug monitoring. Novartis alleged a breach of Clause 3.2 as the promotion was outside the terms of the marketing authorization.

Additionally, Novartis considered dose adjustments were a derivative of blood level monitoring and blood level monitoring to be a requirement of the terms of the marketing authorization. To claim that no dose adjustments were required when switching and emphasising this claim in bold text in a bright colour, created the perception that close blood level monitoring was not necessary or less important and thus misled the reader by implication and put the patient at risk of an inadvertent switch.

Novartis alleged that this indirect misleading of the reader by implication was in breach of Clause 7.2.

Novartis noted that failing to carry out appropriate close monitoring of patients could lead to potential toxicity or underdosing with serious clinical implications including graft loss or death. If readers were misled into thinking that dose for dose switching was advocated and that close monitoring was not important, it was not unreasonable to infer that some practitioners might be less rigorous with the necessary close monitoring, especially those not directly involved in the daily care of transplantation patients, like community pharmacists and thereby putting patients at risk of serious clinical implications, particularly in the community.

RESPONSE

Dexcel submitted that Deximune had been demonstrated to be bioequivalent to Neoral. This was confirmed by healthy volunteer studies under fed and fasting conditions. The data from these studies was included in the Deximune SPC. In addition, a post-marketing, retrospective, parallel, multicentre survey in transplant patients receiving these two formulations had compared their toxicity profiles and bioavailability (Berger *et al* 2008). Of the patients reviewed, 157 out of the 174 included received both products; Neoral was administered first and then the patients were transferred to Deximune. Ciclosporin blood level measurements were taken on three occasions during the review period. The results confirmed the bioequivalence of the two products in this patient population using analytical programs which took account of the patient variables. In addition, the products were deemed to have similar toxicity profiles and as a result the investigators concluded that the two products could be interchanged without the need for dosage adjustment while monitoring blood levels, blood pressure and renal function, all of which were recorded in the study.

Deximune was currently the only alternative brand of ciclosporin available in the UK. Therefore the only switching that was likely to occur between oral formulations of ciclosporin was between Neoral and Deximune. UK patients were last switched from one formulation of ciclosporin to another when Neoral was introduced; over a period of time the majority of patients were switched from Sandimmune to Neoral. Dexcel understood from prescribers that patients were switched on a dose for dose basis and due to lack of bioequivalence, this resulted in changes in trough ciclosporin levels and rejection episodes for a number of patients. As a result, a significant number of prescribers had been concerned about the appropriate dose to start patients on Deximune, either *de-novo* or when switching from Neoral.

In the light of the bioequivalence information outlined above and prescribers' concern about the appropriate starting and switching dose for Deximune, this was an important issue that needed to be addressed. It was important from a safety point of view therefore to highlight the fact that when starting new patients on Deximune or when transferring patients from Neoral to Deximune, the dose should be the same as for Neoral. For this reason, the claim 'However patients can be started on Deximune or switched to Deximune from Neoral without the need for dose adjustment' was highlighted in the text to minimise the risk that a patient might be transferred on a higher or lower dose and so potentially be at risk of rejection or toxicity.

Dexcel noted Novartis' allegation that it had not been made it clear to the reader that patients switched from Deximune to Neoral should be closely monitored for a period following the switch. Dexcel noted that it was clearly stated in the mailing that 'Because of the differences in absorption between fed and fasted patients with previous formulations of ciclosporin, the current recommendations are for close monitoring when switching any formulation of ciclosporin'. This statement immediately preceded the one regarding the starting dose which Dexcel considered was the appropriate positioning from a patient safety point of view. Dexcel had never, either verbally or in writing, suggested that Neoral patients should be switched to Deximune without close monitoring to confirm ciclosporin blood levels, renal function and blood pressure.

In December 2009 at the request of the MHRA, Dexcel sent a 'Dear Healthcare Professional' letter to 54,364 health professionals including: GPs; retail and hospital pharmacists; hospital doctors (from

staff grade to professors) within dermatology, nephrology, paediatric nephrology, renal, rheumatology and transplant and pharmaceutical advisors in primary care trusts. This letter was approved by the MHRA and could be viewed on its website. The letter clearly highlighted the need to prescribe ciclosporin by brand, for close monitoring to be carried out when switching and that transplant patients should not have their brand of ciclosporin changed without the permission of the prescriber. This was the only communication that Dexcel had had with the majority of these health professionals.

By contrast, the mailing at issue was sent only to hospital consultants in renal medicine, transplantation and dermatology; hospital pharmacists; pharmaceutical advisors and medicines management pharmacists within primary care trusts; a total of 3,890 health professionals. The letter had also been used subsequently at the British Renal Association/Renal Society joint meeting in May, The British Association of Dermatology meeting in July and in discussions with professionals who fell within the above groups. It was reasonable to assume that these professionals were well informed on the need for close monitoring when prescribing ciclosporin for patients, particularly when switching between brands. However, as noted above, Dexcel considered it appropriate to remind them of the need for close monitoring when switching between brands. In addition, at no time after the mailing was sent or in subsequent 1:1 conversations had any health professional complained to Dexcel about the content of this mailing. Furthermore, in the 10 months that Deximune had been available in the UK Dexcel had had no reports of an adverse reaction as a result of a patient being switched from Neoral to Deximune.

Dexcel appreciated that Novartis would be concerned about an alternative brand of ciclosporin being available in the UK. Dexcel aimed to promote Deximune in a responsible manner and in doing so it hoped to provide prescribers with the appropriate information for them to make an informed choice on how and when to choose Deximune. Decisions about ciclosporin prescribing were in the main made by hospital consultants, hospital pharmacists, primary care medicines management pharmacists and senior managers at hospital and PCT level. As a result, Dexcel's promotional activity had been mainly directed at these individuals.

In Dexcel's promotion of Deximune it had looked to convince the decision makers to make an informed choice based on the clinical evidence and the cost effectiveness for Deximune. Dexcel had always taken patient safety into account and it had never promoted Deximune outside of the scope of the SPC. Dexcel did not believe that the mailing at issue was in breach of Clauses 3.2 or 7.2 and trusted that having considered Dexcel's response the Authority would agree.

PANEL RULING

The Panel noted that it had considered a closely similar complaint in Case AUTH/2338/7/10. The complaint in Case AUTH/2340/7/10 had been received before Case AUTH/2338/7/10 had been completed and so Case AUTH/2340/7/10 was allowed to proceed. The Panel referred to its ruling in Case AUTH/2338/7/10 with regard to the alleged breaches of Clauses 3.2 and 7.2.

Case AUTH/2338/7/10

The Panel noted that the mailing at issue (DEX/10/0013) featured a number of claims in bold, bright blue font. One of these was 'There is no significant difference between the absorption of ciclosporin from Deximune and Neoral under fed and fasted conditions'. This was immediately followed, in plain, black type by the next paragraph which began 'Because of the differences in absorption between fed and fasted conditions with the previous formulations of ciclosporin the current recommendations are for close monitoring when switching any formulation of ciclosporin'. This was, in turn, followed by another claim in bold, bright blue font that 'However, patients can be started on Deximune or switched to Deximune from Neoral without the need for dose adjustment'.

The Deximune SPC stated the following:

> 'Due to differences in bioavailability between different oral formulations of ciclosporin it is important that health professionals and patients be aware that substitution of Deximune Capsules for other formulations may lead to alterations in ciclosporin blood levels.
>
> Therefore patients should not be transferred to or from other oral formulations of ciclosporin without appropriate close monitoring of ciclosporin blood concentrations, serum creatinine levels and blood pressure.'

The Panel noted the presentation and layout of the mailing and considered that the reader's eye would be drawn to the claims in bright blue text such that they were likely to overlook the statement inbetween about the current recommendations for close monitoring. In the Panel's view, however, the statement regarding monitoring was, in any case, insufficient in that the Deximune SPC specifically referred to the close monitoring of ciclosporin blood concentrations, serum creatinine levels and blood pressure. The Panel noted that although the mailing had been used with hospital consultants, it had also been used widely with non-specialist health professionals. In the Panel's view, although some of the target audience would be experienced and knowledgeable about the use of ciclosporins, and thus familiar with content of the SPCs with regard to switching, others would not and so detailed knowledge in that regard should not be assumed. Overall, the Panel considered that the mailing was misleading with regard to the precautions

necessary when switching a patient from Neoral to Deximune. A breach of Clause 7.2 was ruled. The Panel considered that the claims were not consistent with the particulars listed in the Deximune SPC. A breach of Clause 3.2 was ruled.

Case AUTH/2340/7/10

The Panel considered that its comments and rulings above applied. Breaches of Clauses 3.2 and 7.2 were ruled.

2 Deximune detail aid (ref DEX/10/0001)

This detail aid was available on-line from www.deximune.co.uk.

COMPLAINT

Novartis noted that on page 5 of the detail aid there was a claim that Deximune had been proved to: 'Be interchangeable with Neoral without the need for dose adjustment'. This was not followed or preceded by any warning about the associated close monitoring required. There was also no mention of the licensed requirement of concurrent serum creatinine and blood pressure monitoring.

The marketing authorization of Deximune clearly stated:

> 'Due to differences in bioavailability between different oral formulations of ciclosporin it is important that health professionals and patients be aware that substitution of Deximune Capsules for other formulations may lead to alterations in ciclosporin blood levels. Therefore patients should not be transferred to or from other oral formulations of ciclosporin without appropriate close monitoring of ciclosporin blood concentrations, serum creatinine and blood pressure.'

There was no mention anywhere in the detail aid of the close monitoring required by the terms of the marketing authorization when switching patients between formulations of ciclosporin.

The Code required the promotion of a medicine to be in accordance with the terms of its marketing authorization and consistent with the particulars listed in the SPC.

Novartis alleged that the lack of inclusion of text warning readers to perform the close monitoring of ciclosporin levels, serum creatinine and blood pressure when switching between different formulations of ciclosporin was in breach of Clause 3.2.

Novartis also believed the Code required claims to be accurate, objective and unambiguous and not to mislead either directly or by implication or by undue emphasis. Additionally, the material must be sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine.

Novartis considered dose adjustments to be a derivative of blood level monitoring and blood level monitoring to be a requirement of the terms of the marketing authorization. Claiming that no dose adjustments were required when switching created the perception that close blood level monitoring was not necessary or less important, and by not providing any additional text to inform the reader of the need for close monitoring this was incomplete and misled the reader and implied that close monitoring when switching patients was not necessary, putting the patient at risk of serious clinical implications.

Novartis alleged that the omission of a statement about close monitoring as well as the indirect misleading of the reader through implication and by not providing any warning about close monitoring when switching, was in breach of Clause 7.2.

The serious clinical implications were highlighted by the MHRA Drug Safety Update 2009. Novartis considered that statements regarding interchangeability between formulations should always be accompanied by a statement about the requirement for close monitoring.

Novartis considered very strongly that the claims above did not adhere to the terms of the marketing authorization either by omission or through undue emphasis and implication, in breach of Clause 3.2.

Novartis also believed that the 'no need for dose adjustment' claim was highly likely to be misinterpreted; some prescribers would be misled into thinking that close monitoring was not important or required during switches, thereby breaching Clause 7.2.

RESPONSE

Dexcel noted that the detail aid was produced in September 2009 when it launched Deximune and reprinted in February 2010 as a result of a price change, without any further changes. The original brochure was one of a number of items which the MHRA viewed as part of the launch activities. At the time the MHRA was satisfied with the detail aid, which included the wording on page five that Novartis had highlighted. The MHRA did not require pre-vetting of any further promotional items.

However, in the light of this complaint and experience with Deximune to date, Dexcel had considered that this item would be improved by the inclusion of information about the need for close monitoring when switching patients from Neoral to Deximune. Dexcel therefore did not contest the complaint and would not circulate or distribute any more copies with immediate effect.

PANEL RULING

The Panel noted that page 5 of the detail aid featured a number of bullet points about Deximune one of which stated that it had been proven to: 'Be interchangeable with Neoral without the need for dose adjustment'. The preceding bullet point stated that it had been proven to: 'Be equivalent to the innovator product, Neoral, under fed and fasted conditions'. There was no statement anywhere in the detail aid that if patients were switched from one brand of ciclosporin to another, close monitoring of ciclosporin blood concentrations, serum creatinine and blood pressure were required.

The Panel noted that the detail aid was available on-line for access by health professionals only. The Panel considered that a very wide audience might access the detail aid including those with little or no detailed knowledge of ciclosporin use. The Panel considered that the detail aid was misleading in its omission of detailed information about switching. A breach of Clause 7.2 was ruled. The Panel considered that the detail aid was not consistent with the particulars listed in the Deximune SPC. A breach of Clause 3.2 was ruled. The Panel noted that Dexcel had not contested the complaint about the detail aid.

Complaint received **29 July 2010**

Case completed **3 September 2010**

CASE AUTH/2344/8/10

ANONYMOUS v SANOFI-AVENTIS

Conduct of representative

An anonymous complainant alleged that a Sanofi-Aventis representative had held an inappropriate discussion with a consultant in the cardiology reception area. The complainant explained that the representative had, *inter alia*, discussed Clexane (enoxaparin) and 'asked' if the consultant would sign a character witness statement in order to obtain a shotgun licence. The complainant stated that such a request, while discussing a product, was entirely inappropriate.

The consultant was, according to the complainant, not an appropriate person to sign the representative's shotgun licence. The complainant was not aware that it was within the guidelines for the consultant to sign such a document given his professional relationship and lack of knowledge of the representative's medical history.

The detailed submission from Sanofi-Aventis is given below.

The Panel noted that according to Sanofi-Aventis the representative had made an appointment to see a doctor with the only objective of asking that doctor to sign Section D of a shotgun licence renewal form. The purpose of the meeting was made clear in advance. The representative had been waiting to see the doctor with whom he had the appointment when another doctor, whom he had known for some time, had started to talk to him. At the request of the representative that doctor had ended up signing the form and afterwards had asked questions about Sanofi-Aventis products. The representative had answered questions about one product and arranged for a colleague to call and answer another. The representative had recorded the call as a 'spec call, share exp with Rx Multaq' and the method of access as 'Rep Request'.

The Panel acknowledged that representatives would inevitably build close relationships with those upon whom they called, particularly those they had known for some years. It was, however, important that such relationships were kept on a professional basis. The Panel queried whether it was acceptable for a representative, in the course of his duty as such, ever to ask someone upon whom he called to do something for him of a private or personal nature. Clear distinctions should be made between personal and business arrangements. Representatives should be aware of the impression created by their conduct.

The Panel considered that the course of events was subject to the Code and was concerned about the impression given by the interaction which took place in the reception area. There were differences between the parties' accounts. However both agreed that the form had been signed and Sanofi-Aventis products had been discussed.

The Panel considered that the representative had not maintained a high standard of ethical conduct in relation to his meeting with the doctor. The Panel queried whether it was ever acceptable for a representative to ask a health professional to sign such a form. It was certainly not acceptable to do so when the meeting had not been pre-arranged, took place in a public area and formed part of a promotional call. A breach of the Code was ruled.

An anonymous complaint was received about the conduct of a Sanofi-Aventis representative. The complainant stated that a number of doctors and administrative staff knew about a call by the representative and a discussion with a consultant which was alleged to be inappropriate.

COMPLAINT

The complainant stated that in the cardiology reception area the representative discussed Clexane (enoxaparin) and requested further calls for another Sanofi-Aventis representative in order to discuss prescribing policy changes. During this call the representative 'asked' if the consultant would sign a character witness statement in order to obtain a shotgun licence. The complainant stated that such a request, while discussing a product, was entirely inappropriate. The cost to the representative of correctly filing such documentation was £30-£50 which was discussed during the meeting.

Secondly, the complainant was very concerned with the latest headlines within the press about recent crimes involving firearms.

The consultant was, according to the complainant, not an appropriate person to sign the representative's shotgun licence. The complainant was not aware that it was within the guidelines for the consultant to sign such a document given his professional relationship and lack of knowledge of the representative's medical history.

When writing to Sanofi-Aventis the Authority asked it to comment in relation to Clauses 9.1 and 15.2 of the Code.

RESPONSE

Sanofi-Aventis stated that it did not doubt the genuine nature of the complaint or underestimate the seriousness of the issue. However, the

complaint was written in the third person rather than being a first person account, and was received two months after the event. Discrepancies had been identified between the content of the letter, Sanofi-Aventis' own interview findings and the factual call record.

Sanofi-Aventis therefore considered it important, not least out of respect for and the need to ensure fairness for everyone involved, that the Panel was provided with as clear a record of events as possible. Sanofi-Aventis had established the following:

- The representative in question visited the cardiology department to meet a doctor.

- The visit had been pre-arranged to occur during the lunch hour, with the sole purpose made clear in advance. The doctor, as a person of professional standing who had known the representative for several years, had agreed to countersign a photograph and Section D of a shotgun licence renewal form. Sanofi-Aventis stated that this was analogous to the signing of photographs and application form for a passport. Contrary to the complainant's submission, it was clear that this request was specifically not one of provision of a medical statement of suitability. Sanofi-Aventis noted that the licensing authority had a duty to request a medical reference from the registered GP.

- There had been no intent to promote any product during the call – it was intended to be a professional-to-professional interaction for a matter unrelated to business, conducted at a time convenient to the doctor.

- On arriving at the department at the arranged time, the doctor was not present. The representative asked the receptionist, whom he knew well from professional interactions, to contact the doctor. The representative was asked to sit and wait. Sanofi-Aventis understood that there were no patients within the reception area at this time.

- Whilst the receptionist tried to contact the first doctor, a second doctor arrived. The representative and that doctor also had a long-standing professional relationship, having known each other for eight years. The doctor recognised the representative, acknowledged him and started a conversation.

- The representative asked the second doctor if he had seen the first doctor, to which he replied 'No'. Due to their long-standing acquaintance, the representative then explained why he was visiting the department, and asked him if he would be prepared to countersign his form. This request was only made because the representative judged that his long-standing relationship with the second doctor was of a sufficient nature to make the request appropriate.

- Upon reading the document the second doctor agreed to sign it and the photograph. No discussion took place whilst this was happening.

- After signing the form, the doctor asked the representative about two Sanofi-Aventis products. The representative answered the questions about the product on which he had been trained. He explained that he could not help with the enquiry about the second product with which he was not familiar but that he could arrange for the appropriate person to visit and provide the information requested. This information was logged in the electronic call record and triggered the visit from another Sanofi-Aventis representative.

- At the end of the visit the representative thanked the doctor for his time and left the department.

- Sanofi-Aventis noted the complainant's reference to recent firearms incidents (in Cumbria and Northumberland), suggesting that the representative's actions were inappropriate given the sensitivity surrounding these events. However, they both occurred after this visit and would not have been relevant to either the thoughts of the representative or anyone overhearing the conversation on 1 June.

Sanofi-Aventis believed this was a true and accurate account of events. With this clarity, the question to be addressed was whether this represented a failure to maintain high standards and of the representative to conduct himself appropriately.

Upon reflection the representative was disappointed in himself and embarassed that this had been brought up. He recognised that this was probably not something that he should have discussed in a public area. This had also prompted Sanofi-Aventis to reconsider whether its own procedures gave sufficiently clear guidance on such matters and the event would be highlighted in order to make appropriate recommendations around this incident.

In mitigation, several factors were relvant. Renewal of a shotgun licence, like a passport, required the countersignature of a professional person with a long-standing relationship with the applicant. There appeared to be no sign of abuse of these long-standing professional relationships in making this request. The visit to obtain this countersignature was arranged properly, agreed in advance and planned at a convenient time at a break in the working day. There was no intent to conduct any business other than obtaining the countersignature and even though a question on a company product was asked, no promotion took place during the visit.

Although the request for countersignature could be seen as misguided, Sanofi-Aventis did not consider that, on balance, standards had been allowed to fall such as to breach Clauses 9.1 and 15.2. Had the request not been made and agreed in the

professional manner that the company understood, or had it been included in a visit in which product promotion had been planned, Sanofi-Aventis would have adopted a different position.

PANEL RULING

The Panel noted that according to Sanofi-Aventis the representative had made an appointment to see a doctor with the only objective of asking that doctor to sign Section D of a shotgun licence renewal form. The purpose of the meeting was made clear in advance. The representative had been waiting to see the doctor with whom he had the appointment when another doctor had started to talk to him. At the request of the representative that doctor had ended up signing the form and afterwards had asked questions about Sanofi-Aventis products. The representative had answered questions about one product and arranged for a colleague to call and answer another. The representative had recorded the call with as a 'spec call, share exp with Rx Multaq' and the method of access as 'Rep Request'.

The Panel acknowledged that representatives would inevitably build close relationships with those upon whom they called, particularly those they had known for some years. It was, however, important that such relationships were kept on a professional basis. The Panel queried whether it was acceptable for a representative, in the course of his duty as such, ever to ask someone upon whom he called to do something for him of a private or personal nature. Clear distinctions should be made between personal and business arrangements. Representatives should be aware of the impression created by their conduct.

Section D of the shotgun licence renewal form referred to a countersignature whereby the person signing certified that they knew of no reason why the applicant should not be permitted to possess a shotgun, that to the best of their knowledge and belief the information given in Section A of the form was true, that the photographs enclosed bore a current likeness to the applicant and that they knew the applicant personally. The notes stated that countersignatories should bear in mind the character, conduct and mental condition of the applicant. In the Panel's view this was not analogous to that which was required from a person countersigning photographs for a passport application as submitted by Sanofi-Aventis.

The Panel considered that the course of events was subject to the Code. The doctor knew the representative as a result of what Sanofi-Aventis described as a long-standing professional relationship. According to Sanofi-Aventis the doctor had started the conversation with the representative. The representative had answered a question and recorded the call as a promotional call. Nonetheless, the Panel was concerned about the impression given by the interaction which took place in the reception area. There were differences between the parties' accounts of the matter. However both agreed that the form had been signed and Sanofi-Aventis products had been discussed.

The Panel considered that the representative had not maintained a high standard of ethical conduct in relation to his meeting with the doctor. The Panel queried whether it was ever acceptable for a representative to ask a health professional to sign such a form. It was certainly not acceptable to do so when the meeting had not been pre-arranged, took place in a public area and formed part of a promotional call. A breach of Clause 15.2 was ruled

With regard to Clause 9.1, the Panel considered that the matter was covered by its ruling of a breach of Clause 15.2. It thus ruled no breach of Clause 9.1.

Complaint received **10 August 2010**

Case completed **23 September 2010**

HEALTHCARE CONSORTIUM v DAIICHI-SANKYO

Conduct of representative

A medicines management team leader complained on behalf of a local healthcare consortium that a Daiichi-Sankyo representative, promoting Olmetec (olmesartan), had stated that the medicines management team was to be disbanded. This was not so and could be construed as misleading GPs so that they would prescribe Olmetec.

The detailed response from Daiichi-Sankyo is given below.

The Panel noted that a general practice manager had reported a conversation they had had with a Daiichi-Sankyo representative. It appeared that the complainant had not been party to that conversation. The practice at issue had not agreed to the disclosure of its identity. When told from which healthcare consortium the complaint had come, Daiichi-Sankyo stated the call record of one representative could match the little information provided.

The Panel noted that whilst the company denied the allegation, one of its representatives had, when accompanied by his manager, asked a practice manager whether the Department of Health White Paper, 'Equity and Excellence: Liberating the NHS', meant that primary care trusts would be disbanded. The representative and his manager were left with the impression that the practice manager would explain the implications of the White Paper to the representative at a later date.

The Panel noted that the White Paper set out the new proposed NHS funding and accountability structure. Given the implications and sensitivity of the issues raised, the Panel considered it was entirely foreseeable that representatives might discuss the White Paper with those they called upon. If representatives raised this matter it was beholden upon the company to ensure that they had been appropriately briefed. The White Paper was published on 12 July; the primary care sales team were briefed on it on 23 September, some 10 weeks after the representative identified by the company spoke to a practice manager about the issue and approximately 4 weeks after the receipt of this complaint. The Panel queried whether representatives should have been briefed on the White Paper earlier given that they were proactively raising it with health professionals.

The Panel considered that on the balance of probabilities the representative had discussed the implications of the White Paper with a practice manager. However, it was not possible to determine on the balance of probabilities whether the representative had stated that the medicines management team would be disbanded as alleged. The parties' accounts differed. The Panel thus ruled no breach of the Code.

A medicines management team leader at a healthcare consortium complained about the conduct of an unidentified representative from Daiichi-Sankyo UK Ltd at a practice within the consortium.

COMPLAINT

The complainant had stated that the healthcare consortium had been informed by one of its practice managers that a Daiichi-Sankyo representative, promoting Olmetec (olmesartan), had told a practice that the medicines management team was to be disbanded. This was incorrect, and could be construed as misleading GPs so they would prescribe Olmetec.

* * * * *

The medical centre at issue did not want to be identified to Daiichi-Sankyo. When told from which healthcare consortium in the UK the complaint came, the company asked for further information before it submitted its response. The complainant did not respond to this request.

* * * * *

When writing to Daiichi-Sankyo, the Authority asked it to consider the requirements of Clauses 7.2 and 15.2 of the Code.

RESPONSE

Daiichi-Sankyo stated that five of its employees worked within the area in question, but based on the minimal information provided it was difficult to accurately identify who might have had the alleged discussion. Daiichi-Sankyo took this allegation very seriously and had conducted an internal investigation based on assumptions; it noted that it could not respond as completely and accurately as it would like to, as it did not fully understand who was involved, when, where, with whom, and whether the complainant was present during the alleged conversation.

Daiichi-Sankyo submitted that 31 practices formed the healthcare consortium in question and it had inspected the notes that had been logged within the company's call reporting system with health professionals based at these practices over the two months preceding the complaint. There was only one record that could match with the little

information provided. On Tuesday, 3 August, this representative, accompanied by his manager, visited a named medical centre and met the practice manager. The representative and the manager recalled that at the outset the representative asked the practice manager 'What do you know about the White Paper?' which had been published by the Department of Health (DoH), 12 July 2010. In the brief conversation that followed the representative and the manager recalled the representative asking whether the proposals in the White Paper meant that primary care trusts (PCTs) would be disbanded. The practice manager didn't know but implied that she would get more information and explain the implications to the representative at a later date. The representative had a very good professional working relationship with this practice manager, and that she had supported his understanding of the local environment in the past so this would not be out of the ordinary. The representative had not met with, or had any communication with this practice manager since 3 August 2010.

The representative explicitly denied 'telling the practice that the medicines management team was to be disbanded'. He claimed that he would only use the phrase 'medicines management team' when asking a health professional what the local medicine management team's opinion was on certain treatments or protocols.

The company strongly believed that the discussion as recalled by the representative and his manager did not constitute a breach of either Clauses 7.2 or 15.2. Daiichi-Sankyo was concerned that the complainant, described as a lead GP, had made allegations based on a conversation at which he was not present, and had not provided any further details or information as requested by the Authority.

Daiichi-Sankyo explained that it had not provided its field based teams with any briefing materials that referred to the disbandment of medicines management teams; however a presentation was delivered on Thursday 23 September to its primary care sales team on the DoH White Paper 'Equity and Excellence: Liberating the NHS'. This was factual in content and did not provide any instruction on how it should be interpreted. This presentation was certified on Monday, 20 September ie some time after the complaint was made. A copy of the presentation and the associated certificate was provided. There had been no other representative briefings associated with the White Paper.

PANEL RULING

The Panel noted that a general practice manager had reported a conversation they had had with a Daiichi-Sankyo representative to their local healthcare consortium. It appeared that the complainant had not been party to that conversation. Via the complainant, the practice at issue had not agreed to the disclosure of its identity to Daiichi-Sankyo although the company did know the geographical region. Daiichi-Sankyo stated that it was consequently difficult to identify the representative at issue. The Panel noted that, as stated in the introduction to the Constitution and Procedure, the names of individuals complaining from outside the industry were kept confidential save in those exceptional circumstances where disclosure was necessary to enable the matter to be properly investigated. Such disclosure was only made with the complainant's consent.

The Panel noted that whilst the company denied the allegation, it had identified and interviewed a representative who, when accompanied by his manager, had asked a practice manager whether the DoH White Paper 'Equity and Excellence: Liberating the NHS' meant that PCTs would be disbanded. The representative and his manager were left with the impression that the practice manager would explain the implications of the White Paper to the representative at a later date.

The Panel noted that the White Paper referred to the establishment of GP commissioning consortia. PCTs were not part of the new proposed NHS funding and accountability structure. Given the huge implications and sensitivity of the issues raised in the White Paper, the Panel considered it was entirely foreseeable that representatives might discuss its implications with health professionals/appropriate administrative staff. If representatives raised this matter it was beholden upon the company to ensure that they had been appropriately briefed. The White Paper was published on 12 July; the primary care sales team received a presentation on it on 23 September, some 10 weeks after the representative identified by the company spoke to a practice manager about the issue and approximately 4 weeks after the company was notified by the Authority about the present complaint. The Panel queried whether representatives should have been briefed on this earlier given that they were proactively raising it with health professionals.

The Panel considered that on the balance of probabilities the representative had discussed the implications of the White Paper with a practice manager. However it was not possible to determine on the balance of probabilities whether the representative had stated that the medicines management team would be disbanded as alleged. The parties' accounts differed. The Panel thus ruled no breach of Clauses 7.2 and 15.2 of the Code.

Complaint received **10 August 2010**

Case completed **29 October 2010**

ANONYMOUS v BRISTOL-MYERS SQUIBB

Promotion of Onglyza

An anonymous and non-contactable GP alleged that Bristol-Myers Squibb was asking its field force to get a GP to prescribe saxagliptin (Onglyza) for a pre-determined number of patients in a given period of time. The field force had to complete a form stating which GP was going to prescribe saxagliptin, for how many patients – within a week, month, etc. GPs were expected to text their representative when they had completed the agreed number of prescriptions.

The complainant was against such pressure from a pharmaceutical company and would treat his patients in the manner that he saw fit, in line with his clinical experience.

The detailed response from Bristol-Myers Squibb is given below.

The Panel noted that the complainant had provided little information on which to enable Bristol-Myers Squibb to investigate the allegation; his identity, the region in which he practised and the identity of the representative were all unknown.

Bristol-Myers Squibb explained that a representative had worked with a GP who had, of his own volition, texted the representative. In order to track potential progress on an ongoing basis representatives might create their own form on which they would reference prescribers who had indicated a willingness to prescribe based on the call. In that regard the Panel noted that it was important that representatives did not use such forms with health professionals. Any material used with health professionals must be certified in accordance with Clause 14 and otherwise comply with the Code.

The completion of a certified form was not necessarily unacceptable. The alleged request for the GP to text the representative when they had completed the agreed number of prescriptions was denied by Bristol-Myers Squibb. The Panel queried whether such a request was necessarily in breach of the Code.

The Panel considered that there was a difference of view between the complainant and the respondent. Even if a representative had asked a doctor to complete a certified form and text data this was not *de facto* a breach of the Code; the nature of the representative's request and the form provided would be crucial. In this case the complainant provided no details about either. Given the information before it, the Panel ruled no breach.

An anonymous and non-contactable GP complained about the promotion of Onglyza (saxagliptin) by representatives of Bristol-Myers Squibb Pharmaceuticals Limited.

Onglyza was indicated in combination with other oral hypoglycaemics in patients with type 2 diabetes to improve glycaemic control. The marketing authorization was held by Bristol-Myers Squibb and AstraZeneca.

COMPLAINT

The complainant alleged that Bristol-Myers Squibb's management was asking its field force to get a GP to prescribe saxagliptin for a pre-determined number of patients in a given period of time. The field force had to complete a form stating which GP was going to prescribe saxagliptin, for how many patients – within a week, month, etc. GPs were expected to text their representative when they had completed the agreed number of prescriptions.

The complainant was against such pressure from a pharmaceutical company and would treat his patients in the manner that he saw fit, in line with his clinical experience in treating diabetes.

When writing to Bristol-Myers Squibb, the Authority asked it to comment in relation to Clauses 9.1, 9.2 and 15.2 of the Code.

RESPONSE

Bristol-Myers Squibb stated that the performance of sales representatives was judged on their ability to demonstrate core behaviours and to achieve a prescription target for their region. Bristol-Myers Squibb tracked the prescription target by monitoring territory and practice level data provided by IMS. No specific requests for actual patient numbers per GP was expected or had been briefed.

Bristol-Myers Squibb provided an outline of the training programme it used for representatives. At no point was pressuring doctors to text in their prescribing of a product described.

It had come to light that at a training meeting in February, attended by a regional business director, a 'sharing good practice' session took place. One representative had worked with a GP using hypothetical patient profiles suitable for saxagliptin based on their glycaemic profile and in accordance with the saxagliptin licensed indications. The GP was pleased with the outcome of the call and, of his own volition, texted the representative with his

findings following on from the visit. This was shared as an example of how a good call could result in a positive outcome for patients, GPs and Bristol-Myers Squibb, but it was not suggested to other representatives that that they should actively seek this type of communication from the health professionals on whom they called.

Neither since the meeting in February, nor before, had briefing or training been developed to institute mandatory texting of results. GPs were free to communicate with representatives using any channels they pleased and there had not been, nor would there be, any plan to coerce them to do so. Representatives were carefully trained on how often and in what manner to communicate with GPs, as per the Code.

Bristol-Myers Squibb stated that its investigation had not identified any person or area from where this recent behaviour could have emanated.

Bristol-Myers Squibb believed that its models of sales training were robust and that high standards had been maintained. Bristol-Myers Squibb therefore denied any breach of Clauses 9.1, 9.2 and 15.2.

In response to a request for further information, Bristol-Myers Squibb stated that it tracked prescription targets by monitoring territory and practice level data by IMS. No specific request for actual patient numbers per GP was expected or had been briefed to the sales team.

As part of their local planning some representatives would estimate the number of prescriptions required to achieve their target. No direction had been given to any representative to request a set number of prescriptions from a single prescriber.

In order to track potential progress on an ongoing basis, representatives might create a tracker on which they would reference those prescribers who had indicated a willingness to prescribe based on the call. This might include a potential number of prescriptions from that prescriber; however this was solely based on feedback from the prescriber and was not driven by the representative or their managers. An example of such a tracker was provided.

During the 'sharing good practice' session at the training meeting in February, a representative stated that they had received an unsolicited text from a GP; however it was made very clear by the representative that this had not been requested and that the GP had sent it of their own volition based on their positive experience with the medicine. The regional business director present at the training session had stated the following:

'The representative concerned was very clear during the good practice session that this has been an isolated case and that the text had not been requested or suggested during the sales call. I followed-up by reinforcing the fact that we should not ask or expect communication of this nature from our HCPs [healthcare professionals], however it was an example of an excellent call which had been specifically focused on the needs of the patient and the GP resulting in extremely unexpected and positive feedback. No direction was given to any team member to replicate the GP text aspect of the good practice or has been since the meeting.'

The local manager involved in the training meeting had categorically stated that no member of his team had proactively requested text communication from any health professionals nor were any attempts made to coerce them to do so. Given the manager's response Bristol-Myers Squibb did not consider it was appropriate to contact the representatives individually. Bristol-Myers Squibb was not aware of any such issues with any other representatives who were not at the meeting. In addition, there was no evidence to link the complaint with this particular event given that the meeting occurred six months before the complaint was received.

Using the sales model, representatives were trained to focus their calls on the individual prescriber's needs and to tailor their calls appropriately.

Within the one-to-one process, the 'commit' phase included 'State action you will take to facilitate changes'. This statement was envisaged to encompass only those activities that would be permissible within the Code and might include, but were not limited to:

- Arranging a follow-up visit with the customer
- Arranging to see another member of the customer's practice or team to support what had been agreed in the call
- Provision of additional data or information as requested by the customer.

A copy of workshop slides was provided. This was an internal Bristol-Myers Squibb training programme and was the only selling skill training representatives received.

Bristol-Myers Squibb submitted that as standard practice, it checked that all representatives joining the company (including on contract) had taken their ABPI examination and if not, that they were entered for it as required under the Code. All representatives were regularly reminded of their responsibilities under the Code and received regular updates (eg field force meetings) on relevant cases and Code changes.

PANEL RULING

The Panel noted that as the complaint was solely about the conduct of a Bristol-Myers Squibb representative it did not consider that it was necessary for AstraZeneca, which co-promoted the product, to respond to the complaint.

The Panel noted that the complainant was anonymous 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 were judged on the evidence provided by the parties.

The Panel noted the complainant alleged that the representatives had been provided with a form to complete stating which GP was going to prescribe saxagliptin and for how many patients. GPs were expected to text their representative when they had completed the agreed number of prescriptions.

The Panel noted that the complainant had provided little information on which to enable Bristol-Myers Squibb to investigate the allegation. The identity of the complainant, the region in which he practised and the identity of the representative were all unknown.

Bristol-Myers Squibb explained that a representative had worked with a GP who had, of his own volition, texted the representative. In order to track potential progress on an ongoing basis representatives might create their own tracker form on which they would reference prescribers who had indicated a willingness to prescribe based on the call. In that regard the Panel noted that it was important that representatives did not use such forms with health professionals. Any material used with health professionals must be certified in accordance with Clause 14 and otherwise comply with the Code.

The Panel considered that representatives would, of course, encourage health professionals to prescribe Onglyza and provided all activity was in accordance with the Code, this was reasonable. The completion of a certified form was not necessarily unacceptable. The alleged request for a GP to text the representative when they had completed the agreed number of prescriptions was denied by Bristol-Myers Squibb. The Panel queried whether such a request was necessarily in breach of the Code.

The Panel was concerned that the sharing of best practice by representatives might lead to difficulties if it resulted in discussions and possible endorsement of practices that were not in accordance with the Code. However, there was no evidence that this was so in this case. The Panel considered that there was a difference of view between the complainant and the respondent. Even if a representative had asked a doctor to complete a certified form and text data to the representative this was not *de facto* a breach of the Code; the nature of the representative's request and the form provided would be crucial. In this case there were no details about either provided by the complainant. On the basis of the information before it, the Panel ruled no breach of Clause 15.2.

The Panel considered that on the material before it Bristol-Myers Squibb had not failed to maintain a high standard nor failed to recognise the special nature of medicines. The Panel ruled no breach of Clauses 9.1 and 9.2.

Complaint received **13 August 2010**

Case completed **20 September 2010**

CASE AUTH/2348/8/10

GENERAL PRACTITIONER v NORGINE

Movicol mailing

A GP complained that a Movicol (polyethylene glycol (macrogol) 3350 plus electrolytes) mailing, sent by Norgine, seriously misrepresented a recent clinical guideline from the National Institute for Health and Clinical Excellence (NICE) detailing the diagnosis and management of idiopathic constipation in children and young people.

The complainant noted that the first page of the gate-folded mailing was 'stamped', 'Breaking news from NICE' followed by 'New recommendations for constipation in children and young people'. The following page was headed 'NICE news for constipated children' below which was the claim 'Movicol Paediatric Plain/Movicol is now recommended as first-line treatment of faecal impaction and chronic constipation in children and young people.

The detailed submission from Norgine is given below.

The Panel noted that the mailing was about the treatment of constipation and faecal impaction in children and young people ie children aged 2-11 years for whom Movicol Paediatric Plain was indicated (for the treatment of faecal impaction, children had to be at least 5 years old) and young people aged 12 years and above for whom Movicol was indicated. The mailing referred to both products and featured the prescribing information for both.

The Panel considered that anyone reading the mailing would assume that NICE had specifically recommended Movicol Paediatric Plain or Movicol as first line treatment of chronic constipation and faecal impaction in children and young people ie both the under and over 12s. This was not so. The relevant NICE quick reference guide included a clinical management section which stated that for disimpaction and for maintenance therapy, polyethylene glycol 3350 plus electrolytes should be offered as first line treatment. A footnote to both recommendations read 'At the time of publication (May 2010), Movicol Paediatric Plain is the only macrogol licensed for children under 12 years that includes electrolytes … Movicol Paediatric Plain is the only macrogol licensed for children under 12 years that is also unflavoured'. Table 4 of the quick reference guide detailed the recommended doses of the paediatric and adult formulations of polyethylene glycol 3350 plus electrolytes and referred to both as unflavoured. The footnote referred to above, that had appeared in the clinical management section, also appeared at the bottom of table 4. The Panel considered that NICE had, in effect, specifically recommended Movicol Paediatric Plain for the under 12s only. It had not specifically recommended any brand of polyethylene glycol 3350 plus electrolytes for the 12s and over ie 'young people' as also referred to in the mailing. The Panel noted that Movicol as referred to in the mailing was lemon/lime flavoured; Movicol Plain was unflavoured. Neither adult formulation of Movicol had been specifically referred to in the NICE quick reference guide. The Panel thus considered that with regard to the treatment of children aged 12 years and over, the mailing was misleading as to the NICE guidance. A breach of the Code was ruled.

A general practitioner complained about a Movicol (polyethylene glycol (macrogol) 3350 plus electrolytes) mailing (ref MO/10/1995) sent by Norgine Pharmaceuticals Limited. The mailing informed health professionals about a recent clinical guideline from the National Institute for Health and Clinical Excellence (NICE) detailing the diagnosis and management of idiopathic constipation in children and young people.

COMPLAINT

The complainant noted that the first page of the gate-folded mailing was 'stamped', 'Breaking news from NICE' followed by 'New recommendations for constipation in children and young people'. The following page was headed 'NICE news for constipated children' below which was the claim 'Movicol Paediatric Plain/Movicol is now recommended as first-line treatment of faecal impaction and chronic constipation in children and young people.

The complainant alleged that the mailing seriously misrepresented the NICE guidance which referred to polyethylene glycol 3350 plus electrolytes.

When writing to Norgine the Authority asked it to respond in relation to Clause 7.2 of the Code.

RESPONSE

Norgine agreed that the wording in the NICE guidance was as the complainant stated. However, Norgine considered the mailing was a promotional item which notified health professionals of the endorsement by NICE of polyethylene glycol 3350 and electrolytes as first line treatment for constipation in children and young people, of which Movicol Paediatric Plain and Movicol were Norgine's brands. As such, Norgine believed this item complied with the Code.

Moreover, NICE qualified the generic polyethylene

glycol 3350 plus electrolytes recommendation with a footer which stated 'At the time of publication (May 2010), Movicol Paediatric Plain is the only macrogol licensed for children under 12 years that includes electrolytes'. This was similarly qualified in the mailing.

Consequently, Norgine believed that the mailing, used in a promotional context, did not breach Clause 7.2 as it provided accurate information reflecting the NICE guidance for the management of constipation in children and young people.

PANEL RULING

The Panel noted that the mailing was about the treatment of constipation and faecal impaction in children and young people. In the Panel's view this patient population included those children aged between 2 years and 11 years for whom Movicol Paediatric Plain was indicated (for the treatment of faecal impaction, children had to be at least 5 years old) and young people aged 12 years and above for whom Movicol was indicated. The mailing referred to both products and featured the prescribing information for both.

The Panel considered that anyone reading the mailing would assume that NICE had specifically recommended Movicol Paediatric Plain or Movicol as first line treatment of chronic constipation and faecal impaction in children and young people ie both the under and over 12s. This was not so. The NICE quick reference guide 'Constipation in children and young people', provided by Norgine, included a clinical management section which stated that for disimpaction and for maintenance therapy, polyethylene glycol 3350 plus electrolytes should be offered as first line treatment. A footnote to both recommendations read 'At the time of publication (May 2010), Movicol Paediatric Plain is the only macrogol licensed for children under 12 years that includes electrolytes … Movicol Paediatric Plain is the only macrogol licensed for children under 12 years that is also unflavoured'. Table 4 of the quick reference guide detailed the recommended doses of the paediatric and adult formulations of polyethylene glycol 3350 plus electrolytes and referred to both as unflavoured. The footnote referred to above, that had appeared in the clinical management section, also appeared at the bottom of table 4. The Panel considered that, given the footnote, NICE had, in effect, specifically recommended Movicol Paediatric Plain for the under 12s only. It had not specifically recommended any brand of polyethylene glycol 3350 plus electrolytes for the 12s and over ie 'young people' as also referred to in the mailing. The Panel noted that Movicol as referred to in the mailing was lemon/lime flavoured; Movicol Plain was unflavoured. Neither adult formulation of Movicol had been specifically referred to in the NICE quick reference guide. The Panel thus considered that with regard to the treatment of children aged 12 years and over, the mailing was misleading as to the NICE guidance. A breach of Clause 7.2 was ruled.

During its consideration of this case the Panel noted that Movicol Paediatric Plain was indicated for the treatment of chronic constipation in children 2 to 11 years of age. It could be used for the treatment of faecal impaction in children from the age of 5. The NICE quick reference guide, however, recommended its use in children aged less than one year old and up to 12 years old. The Panel noted that the NICE quick reference guide stated as a footnote that '[Movicol Paediatric Plain] does not have a UK marketing authorization for use in faecal impaction in children under 5 years or for chronic constipation in children under 2 years. Informed consent should be obtained and documented'. The mailing featured the same footnote. The Panel queried whether, by referring to the NICE guidance, which it knew recommended the use of Movicol Paediatric Plain in patients for whom it was not licensed, and including the footnote, Norgine had in effect promoted Movicol Paediatric Plain beyond the scope of its marketing authorization.

The Panel further noted that with regard to the adult formulation of polyethylene glycol 3350 plus electrolytes (unflavoured) the NICE quick reference guide stated that for disimpaction in a child/young person 12-18 years of age the dose should be 4 sachets on the first day, then increased in steps of 2 sachets daily to a maximum of 8 sachets daily. The Movicol summary of product characteristics (SPC), however, stated that the dose was simply 8 sachets daily.

The Panel requested that Norgine be advised of its concerns.

Complaint received **16 August 2010**

Case completed **23 September 2010**

ANONYMOUS PRACTICE NURSES v NOVO NORDISK

Conduct of representative

An anonymous and non-contactable group of practice nurses complained about the activities of two representatives, one of whom worked for Novo Nordisk whilst the other worked for a devices company.

The complainants stated that the Novo Nordisk representative, who was well known to them, could be a regular nuisance, just walking into their rooms and ignoring receptionists. The representatives were now both going around together promoting their different products at the same time and their visits were less than informative. They asked if they could record a visit as a works call and said they were under pressure to see so many people per day but the complainants often got follow-up marketing survey calls and felt they would be put on the spot particularly if no medicines or devices had been mentioned as was often the case. They had both said their managers knew they did this which the complainants found extraordinary.

Surely it was illegal for two representatives from different companies to call on health professionals together and promote each of their products? The complainants stated that they had been driven to complain because the Novo Nordisk representative was attending daytime and evening meetings held by the other representative, particularly in local hospitals throughout June and July. At these meetings the Novo Nordisk representative got involved with laboratory personnel and nurses regarding the features and quality control of the devices of the second company. The complainants believed that as a Novo Nordisk representative she was not trained to do this and some of the staff had no idea that she didn't work for the devices company.

The detailed response from Novo Nordisk is given below.

The Panel noted that the complainants were anonymous and non-contactable. As set out in the introduction to the Constitution and Procedure, the 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 Panel noted that there were some differences in detail between the parties' accounts. It was difficult in such circumstances to determine precisely what had occurred. The Panel noted that the Novo Nordisk representative had denied the allegations that she had walked into rooms and ignored receptionists, falsified call records in order to meet call rate targets or discussed features of the second company's devices. The representative had, however, held two joint meetings with the second company's representative but these were at lunchtime in GP surgeries and not in the evening or at the hospitals identified by the complainants. The representative had only provided 'maintenance of relationship' cover for the hospitals mentioned by the complainants, whilst the usual representative was on sick leave.

The Panel noted that it was not a breach of the Code *per se* for representatives from different companies to hold joint meetings and each promote their own company's products provided all of the arrangements complied with the Code. The Panel noted the allegation that the Novo Nordisk representative, when on her own, would walk into the complainants' rooms and ignore receptionists. The Panel was concerned that the complainants alleged that the representatives' visits were less than informative. The representative had denied this allegation. In this regard the Panel noted in particular the requirements of the Code that representatives must ensure that, *inter alia*, the manner in which calls were made on health professionals did not cause inconvenience. The wishes of individuals on whom representatives wished to call and the arrangements in force at any particular establishment, must be observed. The Panel queried why the complainants continued to see the representatives if they were so concerned about their activities. Novo Nordisk had not provided any information about the role of the manager who, according to the complainants, knew about the representatives' activities.

The Panel considered that there was insufficient evidence before it to determine on the balance of probabilities that a breach of the Code had occurred. No breach was thus ruled.

An anonymous and non-contactable group of practice nurses complained about the activities of two representatives who were alleged to go around together promoting their products. One worked for Novo Nordisk Limited and the other for a devices company. The Director decided that the complaint about the representative employed by the devices company should not proceed as the representative promoted devices which were not medicines and were not covered by the Code.

COMPLAINT

The complainants stated that they were becoming

increasingly frustrated by two representatives who worked for different companies but who were going around together promoting their products. The complainants all had an interest in diabetes but were feeling uncomfortable and were sure the representatives' practice was unethical.

The Novo Nordisk representative was well known to the complainants; on her own she could be a regular nuisance, just walking into their rooms and ignoring receptionists. The second representative was employed by a devices company and had been introduced to most of the complainants by the first representative as they used to be colleagues at Novo Nordisk. They were now both going around together promoting their different products at the same time and their visits were less than informative. They asked if they could record a visit as a works call and stated that they were under pressure to see so many people per day but the complainants often got follow-up marketing survey calls and felt they would be put on the spot particularly if no medicines or devices had been mentioned, as was often the case. It was becoming a real concern and they had told the representatives that they needed to be careful as they might get into trouble. They had both said their managers knew they did this which the complainants found extraordinary. The complainants did not know of any other representatives who went around together like this so they were not sure what to do.

Surely it was illegal for two representatives from different companies to call on health professionals together and promote each of their products as it also took up a lot of time particularly as they were now in the holiday season and short staffed? They had been driven to complain because the Novo Nordisk representative was also going along to daytime and evening meetings held by the second representative particularly into the local hospitals throughout June and July which some of the complainants attended. These were hospital meetings for the devices company but the Novo Nordisk representative was there too and got quite involved with laboratory personnel and nurses regarding the features and quality control of the devices of the second company. The complainants believed that as a Novo Nordisk representative she was not trained to do this and some of the staff had no idea that she didn't work for the devices company. The Novo Nordisk representative was not a hospital representative so they wondered why she was there at all. They were also aware from other colleagues that this was also happening in a different area; a number of the complainants worked very closely with the specialist nurses in all the hospitals at issue and they had recently shared their concerns too. As Novo Nordisk had a hospital representative assigned to these hospitals this was very confusing for them.

When writing to Novo Nordisk the Authority asked it to respond in relation to the requirements of Clauses 2, 9.1, 15.2 and 15.4 of the Code.

RESPONSE

Novo Nordisk submitted that from January to June 2010 its representative had promoted Victoza to primary care health professionals; from July 2010 she had additionally promoted Novo Nordisk's insulin portfolio to the same audience. From mid March 2010 to mid August 2010 she also provided secondary care cover for three local hospitals while the usual sales representative was on long-term sick leave.

The representative had been interviewed and those who conducted the interview were satisfied by her answers and believed she had been open and honest with regard to all aspects of the complaint. She strongly denied all of the complainant's allegations other than the reference to two pre-arranged joint meetings which she organised with the second representative.

With regard to the allegation that the representative was a regular nuisance and just walked into rooms and ignored receptionists, Novo Nordisk submitted that it instilled very high standards of behaviour in the field force and would never condone ignoring receptionists or barging into consulting rooms. The representative denied this allegation.

During the investigation, the representative confirmed two joint meetings had been held with the second representative but she strongly refuted the allegation that she, together with the second representative, had made promotional one-to-one calls with health professionals. She also refuted the allegation that she had ever falsified calls in order to meet call rate targets. While call plan compliance (the number of customers seen according to plan) was an important aspect of the sales representative's role, it was not something sales representatives were measured on in terms of bonus or salary.

The representative confirmed that two joint meetings were arranged by her and the second representative. Both were lunchtime meetings at local GP practices where she presented the Novo Nordisk product portfolio. This was followed by the second representative who presented on devices. Each presented on their products separately whilst the other observed. Neither meeting was held in the evening or in the hospitals mentioned by the complainants. The meetings were pre-arranged with the agreement of the GP practices concerned, and were openly and clearly communicated. Pre-arranged joint meetings of this nature was not unusual, however Novo Nordisk sales representatives had been informed that in such circumstances both companies were jointly responsible for complying with the Code.

The representative denied the allegation that she got quite involved with laboratory personnel and nurses regarding the features and quality control of the other representative's devices. The only joint meetings which were held were in GP practices;

laboratory personnel would not have attended given the meetings were not in hospitals. The representative also denied the allegation that she discussed the features of the devices company's product at the above meeting. As stated by the complainants, the Novo Nordisk representative was not trained to discuss such products, nor did she have a desire or need to discuss such products.

Novo Nordisk explained that from mid March until August 2010, its representative had covered three local hospitals as the representative who usually covered these hospitals was on long-term sick leave. However, this cover entailed a 'maintenance of relationship' role, simply providing materials as and when needed, rather than areas which formed part of the representative's targets and no joint meetings with its representative were organised at these hospitals during this period of cover.

Novo Nordisk provided details of the contact rates in primary care. These being three for contact with practice nurses. The contact rates were within the industry average. The targets should be very achievable for an experienced representative. These representatives were not bonused against activity rate but against sales volume vs target.

In conclusion, Novo Nordisk denied breaches of Clauses 2, 9.1, 15.2, 15.4 or any other clauses of the Code.

PANEL RULING

The Panel noted that the complainants were anonymous and non-contactable. As set out in the introduction to the Constitution and Procedure the 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 Panel noted that there were some differences in detail between the parties' accounts. It was difficult in such circumstances to determine precisely what had occurred. The Panel noted that the company had interviewed the representative at issue who had denied the allegations that she had walked into rooms and ignored receptionists, falsified call records in order to meet call rate targets or discussed features of the devices company's products. The representative had, however, held two joint meetings with the devices company's representative but these were at lunchtime in GP surgeries and not in the evening or at the hospitals identified by the complainants. The representative had only provided 'maintenance of relationship' cover for the three hospitals mentioned by the complainants, whilst the usual representative was on sick leave.

The Panel noted that it was not a breach of the Code *per se* for representatives from different companies to hold joint meetings and each promote their own company's products provided all of the arrangements complied with the Code. The Panel noted the allegation that the representative in question when on her own would walk into the complainants' rooms and ignore receptionists. The Panel was concerned that the complainants alleged that the representatives' visits were less than informative. The representative had denied this allegation. In this regard the Panel noted in particular the requirements of Clause 15.4 that representatives must ensure that, *inter alia*, the manner in which calls were made on health professionals did not cause inconvenience. The wishes of individuals on whom representatives wished to call and the arrangements in force at any particular establishment, must be observed. The Panel queried why the complainants continued to see the representatives if they were so concerned about their activities. Novo Nordisk had not provided any information about the role of the manager who, according to the complainants, knew about the representatives' activities.

The Panel considered that there was insufficient evidence before it to determine on the balance of probabilities that a breach of the Code had occurred. No breach of Clauses 2, 9.1, 15.2 and 15.4 were thus ruled.

Complaint received **18 August 2010**

Case completed **20 September 2010**

CASE AUTH/2353/8/10

VOLUNTARY ADMISSION BY NAPP

Provision of business class travel

Napp Pharmaceuticals voluntarily admitted that it had provided business class air travel to delegates attending a congress and that the arrangements had not been certified.

The Authority's Constitution and Procedure provided that the Director should treat an admission as a complaint if it related to a potentially serious breach of the Code. The Director considered that the matters disclosed were potentially serious and the admission was accordingly treated as a complaint.

Napp stated that it had supported 17 health professionals to attend an international congress in Montreal. Napp's congress team had tried to reserve premium economy seats as stipulated in the company's standard operating procedure (SOP) but as none were available, business class seats were reserved. Approval to book these seats was sought from Napp's legal department. In doing so, the meetings department wrongly referred to an SOP which permitted business class flights when travel for delegates was over 4 hours. In fact the SOP stated that 'economy plus' was acceptable for flights exceeding 4 hours. Business class was permitted for health professionals who were providing consultancy services. Approval to book the flights was granted, with the legal team being left with the impression that the flights were for consultants. Unfortunately the reservation of business class travel was not submitted for final certification. This unfortunate outcome was the result of a breakdown in internal communication and not a wilful attempt to flout the Code.

The fact that business class flights had erroneously been booked was only recognised three days before departure. In response to this, Napp's congress team tried to re-arrange the flights but despite checking with a number of airlines, direct premium economy and economy flights from London to Montreal were fully booked. Indirect flights were also checked, but the number of changes involved would have hugely disrupted the delegates' travel plans and their attendance for the duration of the congress. Napp therefore concluded that it would have damaged its reputation, and potentially that of the industry, more to require its delegates to change their travel plans on the outward bound journey at this very late stage.

All return flights, however, were rearranged and delegates were allocated economy seats on indirect flights back to London. Delegates were informed of the mistake in a letter (provided), which also advised them that their return journey had been changed. The revised travel arrangements, however, were not acceptable to 16 of the 17 delegates who had various clinical or travel commitments to fulfil on their return to the UK. These delegates thus returned business class as previously arranged.

Napp took compliance very seriously; this was a genuine oversight and Napp had tried to rectify the situation being mindful of the need to minimise the inconvenience to the health professionals concerned. In addition, the process for the certification for international meeting arrangements was being reviewed to ensure that this mistake did not occur in the future. Extra bespoke training on the Code as it related to delegates, consultants and meeting arrangements would be provided to the congress team.

However, Napp appreciated that the circumstances described above potentially breached the Code in relation to the provision of business class flights to delegates attending an educational meeting and the failure to certify the final travel arrangements.

The detailed response from Napp is given below.

The Panel noted that the Code stated that companies should only offer or provide economy air travel to delegates sponsored to attend meetings. Napp had provided business class travel to delegates sponsored to attend an international meeting in Canada. The Panel further noted that Napp had admitted that the delegates' final travel arrangements had not been certified. Breaches of the Code were ruled.

The Panel noted that potential delegates had not been offered sponsorship to include business class flights to Montreal and that at the outset the congress department had tried to book premium economy seats. As these were unavailable the congress department had sought approval from legal to book business class seats and misquoted the relevant SOP which clearly stated that economy fares (or economy plus fares for flights of longer than four hours) should be booked. Unfortunately the congress department's error in requesting the upgrade was further compounded by the legal department which granted approval on the mistaken basis that those travelling were consultants to the company. The Panel did not have details of the interaction between the two departments but noted that it appeared to have been conducted by email and in that regard the Panel queried how detailed the discussion had been. The congress team proceeded to book the business class flights and assumed that given the involvement of legal department, it did not need to

get the travel arrangements otherwise formally certified.

The Panel noted that the first the delegates would have known about the business class flights was in a letter dated 4 weeks before departure. The delegates were thus not attracted to the meeting on the basis of the class of air travel to be provided. It was, however, unacceptable that given the unavailability of the intended tickets, Napp's internal communications, processes and procedures had subsequently failed. The Panel considered that, notwithstanding the availability of tickets, the requirements of the Code should have been well known to the congress department. In that regard the Panel considered that Napp had been badly let down by its staff. However, the Panel noted Napp's submission that the relevant SOP at the time was not sufficiently clear about the need to certify arrangements for international meetings. This was unacceptable and might have been one of the factors which led to the congress department's mistake not being picked up. The Panel considered that overall high standards had not been maintained. A breach of the Code was ruled.

The Panel noted that following the incident, Napp had rewritten one of the SOPs, to ensure that the need to certify arrangements relating to delegates' attendance at overseas meetings was clear, and had also arranged bespoke training for the congress department.

The Panel noted its comments above and further noted that Napp had given each delegate a letter which stated that the outbound travel arrangements did not comply with the Code. Delegates were further informed that the inbound flights would have to be changed. The Panel noted that the delegates flew home as previously arranged due to clinical/travel arrangements on their return. The Panel considered that the failure of Napp's policies and procedures demonstrated a lack of control in relation to the certification of all of the arrangements for overseas meetings and a lack of awareness of the relevant requirements of the Code. It was of concern that the relevant SOPs were not clear on this matter. The Panel considered that the incident was wholly unacceptable and brought discredit upon or reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

During its consideration of this case the Panel noted Napp's reference to premium economy tickets. The Code specifically referred only to the provision of economy air travel. There had never been any ruling under Code regarding the acceptability or otherwise of premium economy air travel. The Code of Practice Appeal Board would make the final decision in that regard if ever a complaint was made and taken to appeal.

Napp Pharmaceuticals Limited voluntarily admitted that it had provided business class air travel to delegates attending a congress in breach of Clause 19.1 of the Code and that the arrangements had not been certified as required by Clause 14.2.

Paragraph 5.4 of the Authority's Constitution and Procedure provided that the Director should treat an admission as a complaint if it related to a potentially serious breach of the Code. The Director considered that the matters disclosed were potentially serious and the admission was accordingly treated as a complaint.

COMPLAINT

Napp stated that it had supported 17 health professionals to attend the 13th World Congress on Pain being held in Montreal from 29 August to 2 September 2010 as delegates. The internal congress department was responsible for booking the delegates' flights and had tried to reserve premium economy seats between London and Montreal, as stipulated in Napp's standard operating procedure (SOP). Unfortunately none were available and so business class seats were reserved. Approval to book these seats was sought from Napp's legal department. In doing so, the meetings department wrongly referred to an SOP which permitted business class flights when travel for delegates was over 4 hours. In fact the SOP stated that 'economy plus' was acceptable for flights exceeding 4 hours. Business class was permitted for health professionals who were providing consultancy services. Approval to book the flights was granted, with the legal team being left with the impression that the flights were for consultants. Unfortunately the details of this change of arrangements were not submitted for final certification. Therefore business class air travel was booked for the delegates and these specific arrangements were not formally certified. This unfortunate outcome was the result of a breakdown in internal communication and was not a wilful attempt to flout the Code.

The fact that business class flights had erroneously been booked was only recognised three days before the departure date. In response to this, Napp's congress team tried to re-arrange the flights to ensure compliance with the Code, specifically Clause 19.1. However, unfortunately at this late stage, despite checking with a number of airlines, direct premium economy and economy flights from London to Montreal were fully booked. Indirect flights were also checked, but the number of changes involved would have hugely disrupted the delegates' travel plans and their attendance for the duration of the congress. Napp therefore concluded that it would have damaged its reputation, and potentially that of the industry, more to require its delegates to change their travel plans on the outward bound journey at this very late stage.

All return flights, however, were rearranged and all delegates were allocated economy seats on return flights from Montreal to London either via Toronto

or Halifax. Delegates were informed of the mistake in a letter (provided), which also advised them that their travel arrangements for the return journey had been changed.

Because of the change in arrival times to the UK, and the fact that at least five of the delegates had to attend clinics on the day they returned to the UK, Napp agreed to continue to try to book direct return premium economy flights while the congress was ongoing, but, should this prove impossible, Napp had agreed that business class flights would be provided to those individuals.

Napp took compliance with the Code very seriously. This was a genuine oversight and Napp had tried to rectify the situation being mindful of the need to minimise the inconvenience to the health professionals concerned. In addition, the internal process for the certification for international meeting arrangements was being reviewed to ensure that this mistake did not occur in the future. Extra bespoke training on the Code as it related to delegates, consultants and meeting arrangements would be provided to the congress team responsible for booking travel arrangements for sponsored delegates.

However, Napp appreciated that the circumstances described above had led to two potential breaches of the Code; Clause 19.1 in relation to the provision of business class flights to delegates attending an educational meeting and Clause 14.2 with regard to the failure to certify the final travel arrangements.

When writing to Napp, the Authority asked it to respond in relation to Clauses 2, 9.1, 14.2 and 19.1.

RESPONSE

Napp reiterated that it had supported 17 health professionals to attend the 13th World Congress on Pain in Montreal from 29 August to 2 September 2010 as delegates. The sponsored delegates were erroneously provided with business class flights and the final travel arrangements for attendance at this international educational meeting were not formally certified. This unfortunate outcome was the result of an internal misunderstanding that the planned arrangements related to health professionals acting as consultants to the company, not delegates to a meeting, and of a failure to recognise that approval by Napp's legal department did not preclude the need for final certification.

With this background in mind, Napp commented specifically with regard to the requirements of Clauses 19.1, 14.2, 2 and 9.1 of the Code.

Clause 19.1: Providing business class air travel to delegates attending an international meeting

The Code stated that companies should only offer or provide economy class air travel to delegates sponsored to attend meetings. Napp recognised that it had inadvertently provided delegates attending an educational meeting with business class air travel.

Clause 14.2: Failure to gain formal certification for the arrangements for an international meeting

The Code stated that all meetings which involved travel outside the UK must be certified in advance. On this occasion, the final arrangements for air travel for the delegates were not certified in advance of the meeting. Review of the SOPs relating to 'UK and overseas 3rd party organised meetings and congresses' (SAM-PRO-005 version 2) and the 'Provision of sponsorship for healthcare professionals to attend training or educational meetings' (SAM-PRO-009 version 2) which were in effect when the flights were booked, revealed that the stipulation for certification for international meeting arrangements was not sufficiently explicit. Therefore, the process relating to the organisation of Napp presence at UK and international congresses had since been reviewed, and the SOP had been completely re-written and simplified to ensure that the process, including the need for certification of arrangements relating to delegate attendance, was clear (SAM-PRO-005 version 3).

In addition, the medical department would train the congress team on the Code as it related to delegates, consultants and meeting arrangements on 24 September. Training on the new SOP would be provided at the same time.

Clause 2: Bringing discredit to, and reducing confidence in the industry

Whilst Napp appreciated that it had breached the Code as outlined above, it emphasised that every effort had been made to ensure that this unfortunate situation was handled in a responsible manner. Once the mistake was identified, attempts were immediately made to source alternative outbound flights. However, making such alternative arrangements at short notice would have disrupted the delegates' travel plans as they would have arrived late and potentially missed the beginning of the congress. Napp concluded that it could have damaged the industry's reputation more if it had required its delegates to change their outbound journey arrangements at this very late stage when the error was not their fault. Napp therefore decided to allow the delegates to travel business class on the outbound journey as planned, and told the Authority about the situation.

With respect to the return journey, Napp's congress team had reserved economy seats for all delegates. However, since those flights involved changing in either Toronto or Halifax and a different arrival time into the UK, during the course of the congress 16 delegates asked to return on the business class flight as originally booked. In Napp's view, all gave valid reasons for the need to be adequately rested following an overnight flight since they had work or travel commitments on the day of arrival. Details were provided. In the circumstances Napp decided

that the only responsible course of action was to allow them to fly business class as arranged. The remaining delegate extended his stay in Montreal post-congress, and a premium economy flight was arranged for his return.

With this in mind, rather than discrediting and reducing confidence in the industry, Napp believed the opposite was true, given the open and honest manner in which this genuine mistake was communicated and managed with the delegates. The Napp personnel involved behaved professionally and responsibly, ensuring that the delegates were not unnecessarily inconvenienced. In addition, on realising the mistake, Napp told the Authority of the potential breaches by way of a voluntary admission. Therefore Napp strongly refuted the claim that by providing business class travel as described above, that it had discredited or reduced confidence in the industry.

Clause 9.1: Failure to maintain high standards at all times

It was extremely unfortunate that this mistake occurred in the organisation of the flight arrangements, and as previously explained this was due to a genuine misunderstanding of information contained within email correspondence and an assumption that the planned arrangements related to consultants working for the company, not delegates to a meeting. It also highlighted a failure to recognise that approval by Napp's legal department did not preclude the need for final certification.

However, Napp strongly believed that the high standards demanded of the industry were demonstrated by the behaviour of its personnel in responding to the circumstances in a manner that ensured the least disruption to the delegates and their participation in the international congress. Furthermore, to avoid any similar incidents in the future, the company had provided the necessary training and ensured that the relevant processes were clearer.

In summary, Napp recognised that by providing business class flights to delegates attending an international educational meeting and failing to certify the final travel arrangements, breaches of Clauses 19.1 and 14.2 had occurred. However, for the reasons outlined above, Napp did not consider that its actions had brought discredit to or reduced confidence in the industry, nor did it believe that high standards had not been maintained. Therefore Napp denied breaches of Clauses 2 and 9.1.

In response to a request for further information, Napp provided a copy of the registration form. This form was completed by the health professional to confirm their interest in attending the meeting, following a verbal invitation from a sales representative. Napp noted that the briefing to the sales team from the congress team with respect to inviting individual health professionals did not specify the class of air travel to be provided to the delegates, and indeed stated 'on receipt of the completed delegate details form I will contact the delegate to confirm their places and arrange appropriate travel etc'. Delegates were emailed with personalised outline information to confirm their attendance, accommodation and air travel arrangements, including connecting flights. The class of air travel to be provided was not stated in this email.

The confirmation letter sent to individual delegates, dated 30 July, confirmed the nature of the sponsorship to be provided. Flight confirmation was also provided with this letter, and was the first time that the majority of delegates (except for one, as outlined below) were told that Napp had booked business class flights.

In summary, the majority of delegates did not know that they would be flying business class until final travel arrangements were confirmed in the letter of 30 July. One exception to this was a delegate who contacted the Napp congress team to specifically ask '… what ticket are we flying with – economy/premium economy/business? It's just that I have a few airmiles which I could use to upgrade if possible'. The response from the congress team confirmed that business class air travel would be provided.

PANEL RULING

The Panel noted that the supplementary information to Clause 19.1 of the Code, Meetings and Hospitality, stated that companies should only offer or provide economy air travel to delegates sponsored to attend meetings. Napp had provided business class travel to delegates sponsored to attend an international meeting in Canada. A breach of Clause 19.1 was ruled.

The Panel further noted that Clause 14.2 of the Code stated that all meetings which involved travel outside the UK must be certified in advance in a manner similar to that provided for by Clause 14.1. The relevant supplementary information stated that the signatories should examine, *inter alia*, the nature of the hospitality and the like. The Panel noted that Napp had voluntarily admitted that the delegates' final travel arrangements had not been certified. A breach of Clause 14.2 was ruled.

The Panel noted that potential delegates had not been offered sponsorship to include business class flights to Montreal. The registration form did not identify the class of air travel. At the outset the congress department had tried to book premium economy seats. As these were unavailable the congress department had sought approval from legal to book business class seats and misquoted the relevant SOP which clearly stated that economy fares (or economy plus fares for flights of longer than four hours) should be booked. Unfortunately the congress department's error in requesting the upgrade was further compounded by the legal

department which granted approval on the mistaken basis that those travelling were consultants to the company. The Panel did not have details of the interaction between the two departments but noted that it appeared to have been conducted by email and in that regard the Panel queried how detailed the discussion had been. The congress team proceeded to book the business class flights and assumed that given the involvement of legal department, it did not need to get the travel arrangements otherwise formally certified. In that regard the Panel noted Napp's submission that at the time the relevant SOP was not sufficiently clear about the need to certify arrangements for international meetings.

The Panel noted that the first the delegates would have known about the business class flights was in a letter dated 30 July (4 weeks before departure). The delegates were thus not attracted to the meeting on the basis of the class of air travel to be provided. It was, however, unacceptable that given the unavailability of the intended tickets, Napp's internal communications, processes and procedures had subsequently failed. The Panel considered that, notwithstanding the availability of tickets, the requirements of Clause 19.1 of the Code should have been well known to the congress department. In that regard the Panel considered that Napp had been badly let down by its staff. With regard to Clause 14.2, however, the Panel noted Napp's submission that the relevant SOP at the time was not sufficiently clear about the need to certify arrangements for international meetings. This was unacceptable and might have been one of the factors which led to the congress department's mistake not being picked up. The Panel considered that overall high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel noted that following the incident, Napp had rewritten one of the SOPs, to ensure that the need to certify arrangements relating to delegates' attendance at overseas meetings was clear, and had also arranged bespoke training for the congress department.

The Panel noted its comments above and further noted that Napp had given each delegate a letter which stated that the outbound travel arrangements did not comply with the Code. Delegates were further informed that the inbound flights would have to be changed. The Panel noted that the delegates flew home as previously arranged due to clinical/travel arrangements on their return. The Panel considered that the failure of Napp's policies and procedures demonstrated a lack of control in relation to the certification of all of the arrangements for overseas meetings and a lack of awareness of the relevant requirements of the Code. It was of concern that the relevant SOPs were not clear on this matter. The Panel considered that the incident was wholly unacceptable and brought discredit upon or reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

During its consideration of this case the Panel noted Napp's reference to premium economy tickets. The Code specifically referred only to the provision of economy air travel. There had never been any ruling under the Code regarding the acceptability or otherwise of premium economy air travel. The Code of Practice Appeal Board would make the final decision in that regard if ever a complaint was made and taken to appeal.

Proceedings commenced	**1 September 2010**
Case completed	**27 October 2010**

CASE AUTH/2359/9/10

PHARMACIST v LINCOLN MEDICAL

Promotion of Anapen

A pharmacist complained about a letter and a detail aid issued by Lincoln Medical which promoted Anapen (adrenaline auto-injector).

The complainant noted that the letter claimed a cost saving, compared with a competitor product, on the basis that Anapen, although more expensive, had a longer shelf-life. As the detail aid specifically referred to a shelf-life of 24 months for Anapen 500mcg auto-injectors, the complainant ordered two. The Anapen that the complainant received from the wholesaler had less than a year's shelf life left; it was part of a batch that left the company with 19 months' shelf life left.

The complainant alleged that the claims made for Anapen with regard to its shelf-life were not accurate and could not be substantiated.

The detailed response from Lincoln Medical is given below.

The Panel noted that one page of the detail aid was headed 'Anapen – Economical for long-term protection'. Above a table of data comparing *inter alia*, shelf life of Anapen with that of Epipen was the unequivocal claim 'Anapen auto-injectors have a longer shelf life than Epipen'. The table of data stated that the shelf life for each presentation of Epipen was 18 months whereas the shelf life for Anapen was 21 or 24 months depending on the presentation. At the bottom of the page was the claim 'With the longer shelf life of Anapen, patients also gain the advantage of lower prescription charges since they may need only one prescription every two years'.

The Panel noted Lincoln Medical's submission that the licensed or approved shelf life left on Anapen started to shorten as soon as the adrenaline solution was put into the syringe, thus a customer would not receive Anapen with the full 21 or 24 months' licensed shelf life still intact. However, depending on delays or otherwise in the supply chain and rate of product turnover the Panel considered that, in theory, a pharmacist could order Anapen and Epipen at the same time from a wholesaler and receive products which had the same amount of shelf life left. In the Panel's view 'shelf life' to a customer meant the amount of time they could keep a product before it went out of date. The impression that a pharmacist might receive Anapen with a full 24 months of shelf life was strengthened by the claim in the detail aid that patients might only need one prescription every 2 years.

The Panel considered that the detail aid was misleading as alleged. The impression that customers would receive Anapen with a 2 year shelf life could not be substantiated. Breaches of the Code were ruled.

Under a sub-heading of 'Anapen has the potential to reduce prescribing costs …' the letter stated 'Anapen has a longer shelf life when compared to Epipen, which means fewer repeat prescriptions per patient …'. The Panel noted its comments above and considered that they also applied here. Breaches of the Code were ruled.

A pharmacist complained about the promotion of Anapen (adrenaline auto-injector) by Lincoln Medical Ltd. The material at issue was a 6 page, gate-folded detail aid (ref ANA/10-013) and a letter.

COMPLAINT

The complainant noted that the letter claimed a cost saving compared with a rival make of adrenaline auto-injector, on the basis that Anapen, although more expensive, had a longer shelf life.

The complainant noted that the letter was accompanied by the detail aid which specifically stated that Anapen 500mcg had a shelf life of 24 months. On this basis, the complainant ordered two Anapen 500mcg auto-injectors for use in the private vaccination clinic at his pharmacy. The order was placed with a wholesaler on 3/09/2010 and delivered the same day. However, the Anapen that the complainant received expired 26/08/2011 ie less than 12 months from the date supplied.

The complainant stated that he contacted Lincoln Medical to explain the situation. The company stated that the batch in question was released with an expiry date of just 19 months. The complainant noted therefore, even if it had been sent to him directly from the manufacturers, there was no way that it would have had the 24 months shelf life as claimed in the detail aid.

The complainant submitted that he made it clear to the company that he had ordered its product on the basis of a claimed 24 month shelf life, and yet it did not seem to be concerned that this claim was at variance to the actual properties of its product. The complainant alleged that the claim did not comply with Clause 7.2 that 'Information…must be accurate', or Clause 7.4 'Any information … must be capable of substantiation'.

RESPONSE

Lincoln Medical was surprised by the complaint

since it was well known that the shelf life for all injectables, as approved by the regulators throughout the world, began from the moment of compounding of the active substance into solution and vial or syringe filling. Shelf life was determined by the regulators from this start point and was then finalised and approved based on stability studies for that substance. Shelf life then was approved as 'X' or as 'Y' and was part of the product licence and indeed the summary of product characteristics (SPC). The Anapen 500 SPC clearly showed this was 2 years ie 24 months.

Lincoln Medical submitted that the complainant was confusing shelf life with labelled life which was of course indicated by labelling for every batch of product produced and released to market. The difference between shelf life and labelled shelf should be known by all pharmacists.

Lincoln Medical noted that the detail aid stated the licensed shelf life for both Anapen and Epipen. These were correct. Anapen had always had a longer licensed shelf life than Epipen due to a longer stability of the solution. This had never been questioned or challenged in any of the 23 countries where both brands were approved and licensed.

Lincoln Medical explained that once the adrenaline powder was compounded, the Anapen syringes were filled and they were then tested to set parameters and criteria and released for build out into the final device. Once built out they were once again tested for functionality and other parameters and batch released to various markets. All of these activities took time and the shelf life clock was running. The same applied to Epipen and all injectables which followed this manufacturing process. Lincoln Medical was proud to provide adrenaline auto-injectors globally with the best possible labelled shelf for all end-users. The company strove to provide best medico-economic value for payers, which in the UK was the NHS. It was able to do this because it started with a longer approved shelf life than that of Epipen which only had 18 months for all of its presentations. Since Epipen had to go through the same or similar release and build out testing it lost approved shelf too, leaving an even shorter labelled shelf.

In summary, Lincoln Medical did not accept that this was a valid complaint and was surprised that the complainant, as a pharmacist, did not know or was seemingly unable to understand the difference between approved shelf life for a compounded solution and labelled shelf which was the reality of what came to the market. Lincoln Medical further noted that the normal UK distribution chain of product going from manufacturer to pharmaceutical wholesaler who then shipped to a pharmacy, whether in a hospital or a high street, made it impossible to absolutely guarantee that full approved shelf life product could be supplied as these products frequently sat on shelves awaiting demand and the labelled shelf got shorter by the day.

Lincoln Medical considered that the complaint was somewhat disingenuous.

In response to a request for further information regarding a letter sent with the mailing, Lincoln Medical stated that the letter was, in fact, not sent to a GP nor was it sent to the complainant but was sent to a very small number of selected chief executive officers of a small number of primary care trusts. Lincoln Medical was thus unsure as to how it came into the complainant's possession.

Lincoln stated that it could not constructively add anything to its earlier comments in this matter and continued to be surprised that the complainant did not know, or seem to know, the difference between shelf life, as approved by regulators and shown in the SPC, and labelled shelf life as shown on a packaged product. It was somewhat disingenuous to expect a compounded solution to be commercially available on the same day as it was compounded, but the shelf life was so allocated by the regulators in the full knowledge that following compounding and filling etc it took time for the solution to be released with labelled shelf life reflecting its remaining life. Comparing shelf life as approved by the regulators for two different compounded solutions was therefore legitimate.

Lincoln Medical submitted that at no time had it compared anything different.

PANEL RULING

The Panel noted that one page of the detail aid was headed 'Anapen – Economical for long-term protection'. Above a table of data comparing the presentation, unit cost and shelf life of Anapen with that of Epipen was the unequivocal claim 'Anapen auto-injectors have a longer shelf life than Epipen'. The table of data stated that the shelf life (not the 'licensed shelf life' as submitted by Lincoln Medical) for each presentation of Epipen was 18 months whereas the shelf life for Anapen was either 21 or 24 months depending on the presentation at issue. At the bottom of the page, beneath another table of data, was the claim 'With the longer shelf life of Anapen, patients also gain the advantage of lower prescription charges since they may need only one prescription every two years'.

The Panel noted Lincoln Medical's submission that the licensed or approved shelf life left on Anapen started to shorten as soon as the adrenaline solution was put into the syringe. It was understandable that a customer would not receive Anapen with the full 21 or 24 months' licensed shelf life still intact. The Panel noted that Epipen only had a licensed shelf life of 18 months. However, depending on delays or otherwise in the supply chain and rate of product turnover the Panel considered that, in theory, a pharmacist could order Anapen and Epipen at the same time from a wholesaler and receive products which had the same amount of shelf life left. In the Panel's view 'shelf life' to a customer meant the amount of time

they could keep a product before it went out of date. The impression that a pharmacist might receive Anapen with a full 24 months of shelf life was strengthened by the claim that patients might only need one prescription every 2 years.

The Panel considered that the detail aid was misleading as alleged. A breach of Clause 7.2 was ruled. The impression that customers would receive Anapen with a full 24 months of shelf life could not be substantiated. A breach of Clause 7.4 was ruled.

The Panel noted that the letter, under a sub-heading of 'Anapen has the potential to reduce prescribing costs and deliver savings to the NHS' stated 'Anapen has a longer shelf life when compared to Epipen, which means fewer repeat prescriptions per patient …'. The Panel noted its comments above and considered that they also applied here. The letter implied unequivocally that the reader would always receive Anapen with a longer shelf life left on it than Epipen. Given the supply chain, this might not always be the case.

The Panel considered that the letter was misleading as alleged. A breach of Clause 7.2 was ruled. The impression that customers would always receive Anapen with a longer shelf life than Epipen could not be substantiated. A breach of Clause 7.4 was ruled.

Complaint received **24 September 2010**

Case completed **4 November 2010**

CODE OF PRACTICE REVIEW – NOVEMBER 2010

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

2234/5/09	**Lilly v Novo Nordisk**	**Promotion of Victoza prior to the grant of its marketing authorization**	**Four breaches Clause 2 Four breaches Clause 3.1 Four breaches Clause 7.2 Four breaches Clause 7.3 Breach Clause 7.9 Five breaches Clause 9.1 Three breaches Clause 12.1 Audit required by Appeal Board Public reprimand by Appeal Board Two re-audits required by Appeal Board**	**Report from Panel to Appeal Board**	**Page 3**
2269/9/09	**Director v Novo Nordisk**	**Breach of undertaking**	**Breaches Clauses 2, 9.1 and 25 Audit required by Appeal Board Public reprimand by Appeal Board Re-audit required by Appeal Board**	**Report from Panel to Appeal Board**	**Page 25**
2308/4/10	**Media/Director v Norgine**	**Lack of sponsorship declaration in published letter**	**Breaches Clauses 9.1, 9.10, 23.2 and 23.8**	**Appeal by respondent**	**Page 30**
2310/4/10	**Novo Nordisk v Lilly**	**Promotion of Byetta**	**Breach Clause 2 Two breaches Clause 3.1 Two breaches Clause 7.2 Two breaches Clause 9.1**	**Appeal by respondent**	**Page 43**
2312/4/10	**Allergan v Pfizer**	**Promotion of Xalatan**	**Breach Clause 3.2 Two breaches Clause 7.2 Two breaches Clause 7.3 Breach Clause 9.1**	**No appeal**	**Page 59**
2317/5/10	General Practitioner v AstraZeneca	Conduct of representative	No breach	No appeal	Page 65
2318/5/10	Specialist Diabetes Registrar v Novo Nordisk	Promotion of Victoza	No breach	No appeal	Page 73
2320/5/10	**Anonymous v AstraZeneca**	**Promotion of Symbicort**	**Two breaches Clause 7.2 Two breaches Clause 7.3 Two breaches Clauses 7.4 Breach Clause 9.1**	**Appeal by respondent**	**Page 77**

2321/5/10	Media/Director v Roche	Promotion of Tamiflu	No breach	No appeal	Page 83
2322/5/10	**Voluntary admission by AstraZeneca**	**Conduct of representative**	**Breaches Clauses 9.1, 15.2 and 18.4**	**Appeal by respondent**	**Page 88**
2324/6/10	**Pfizer v Johnson & Johnson**	**Promotion of Nicorette**	**Breaches Clauses 7.2, 7.8 and 9.1**	**No appeal**	**Page 96**
2325/6/10	Doctor v Boehringer Ingelheim	Journal 'Special report'	No breach	Appeal by complainant	Page 101
2326/6/10	**Consultant Haematologist v Bayer Schering Pharma**	**Envelope for Kogenate mailing**	**Breach Clause 9.1**	**No appeal**	**Page 105**
2328/7/10	Trust Clinical Director v Pfizer	Conduct of representative	No breach	No appeal	Page 108
2329/7/10	Astellas Pharma Europe v Genus	Eczmol journal advertisement	No breach	No appeal	Page 111
2330/7/10	**Anonymous v Grünenthal**	**Promotion of unlicensed indication in poster presentation**	**Breaches Clauses 2, 3.2 and 9.1**	**No appeal**	**Page 115**
2331/7/10	**Novo Nordisk v Lilly**	**Promotional meeting**	**Breaches Clauses 3.2, 7.2 and 7.10**	**No appeal**	**Page 119**
2332/7/10	**Anonymous v Grünenthal**	**Versatis poster presentation**	**Breaches Clauses 2 and 7.2 Two breaches Clause 9.1**	**No appeal**	**Page 123**
2334/7/10	**Norgine v Movetis**	**Promotion of Resolor**	**Breaches Clauses 3.2, 7.2 and 7.10**	**Appeal by respondent**	**Page 127**
2336/7/10	**Anonymous Medical Contractor v GlaxoSmithKline**	**Alleged unprofessional promotional practices**	**Breach Clause 7.11 Two breaches Clause 9.5**	**No appeal**	**Page 131**
2337/7/10	**Merck Serono v Sandoz**	**Press release and article on Omnitrope**	**Breach Clause 7.2**	**No appeal**	**Page 135**
2338/7/10	**ESPRIT v Dexcel Pharma**	**Deximune mailing**	**Breaches Clauses 3.2 7.2 and 9.1**	**No appeal**	**Page 141**
2340/7/10	**Novartis v Dexcel Pharma**	**Promotion of Deximune**	**Two breaches Clause 3.2 Two breaches Clause 7.2**	**No appeal**	**Page 145**
2344/8/10	**Anonymous v Sanofi-Aventis**	**Conduct of representative**	**Breach Clause 15.2**	**No appeal**	**Page 151**
2345/8/10	Healthcare Consortium v Daiichi-Sankyo	Conduct of representative	No breach	No appeal	Page 154
2347/8/10	Anonymous v Bristol-Myers Squibb	Promotion of Onglyza	No breach	No appeal	Page 156
2348/8/10	**General Practitioner v Norgine**	**Movicol mailing**	**Breach Clause 7.2**	**No appeal**	**Page 159**
2349/8/10	Anonymous group of practice nurses v Novo Nordisk	Conduct of representative	No breach	No appeal	Page 161
2353/8/10	**Voluntary admission by Napp**	**Provision of business class travel**	**Breaches Clauses 2, 9.1, 14.2 and 19.1**	**No appeal**	**Page 164**
2359/9/10	**Pharmacist v Lincoln Medical**	**Promotion of Anapen**	**Two breaches Clause 7.2 Two breaches Clause 7.4**	**No appeal**	**Page 169**

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 sponsorship of promotional meetings
- the sponsorship of scientific and other meetings, including payment of travelling and accommodation expenses
- all other sales promotion in whatever form, such as participation in exhibitions, the use of audio-cassettes, films, records, tapes, video recordings, electronic media, interactive data systems, the Internet and the like.

It also covers:

- the provision of information to the public either directly or indirectly, including by means of the Internet
- relationships with patient organisations
- the use of consultants
- non-interventional studies of marketed medicines
- grants and donations to institutions.

Complaints submitted under the Code are considered by the Code of Practice Panel which consists of the three members of the Code of Practice Authority acting with the assistance of independent expert advisers where appropriate. Both complainants and respondents may appeal to the Code of Practice Appeal Board against rulings made by the Panel. The Code of Practice Appeal Board is chaired by an independent legally qualified Chairman, Mr William Harbage QC, and includes independent members from outside the industry.

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 about the promotion of medicines, or the provision of information to the public, should be sent to the Director of the Prescription Medicines Code of Practice Authority, 12 Whitehall, London SW1A 2DY

telephone 020 7747 8880
facsimile 020 7747 8881
by email to: complaints@pmcpa.org.uk.