PRESCRIPTION MEDICINES
CODE OF PRACTICE AUTHORITY

CODE OF PRACTICE REVIEW

NUMBER 56 MAY 2007

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.

Code Awareness Day 2007

Fifty-five pharmaceutical companies across the UK participated in Code Awareness Day on 15 May. Code Awareness Day is part of an ongoing campaign to increase understanding of the ethical standards that the industry must meet when dealing with health professionals and others.

On Code Awareness Day, pharmaceutical sales representatives and other industry employees who contacted health professionals, patient organisations, professional bodies, the media, members of the public and MPs dedicated time to raising awareness of the Code. Nurses and pharmacists were particularly targeted alongside doctors this year. Many companies also promoted the Code to staff internally and undertook activities in their local area.

In addition:

- A targeted media campaign secured approximately 20 placed features across the medical, pharmaceutical and nursing press.
- An NHS Confederation Briefing on the Code was distributed to all NHS Confederation members and the NHS Alliance sent information about the Code to their members.
- The NHS Alliance, National Association of Primary Care (NAPC) and Royal College of Nursing (RCN) included information in their newsletters and on their websites about the Code throughout May.
- Information about Code Awareness Day was sent to all members of the Health Select Committee and approximately 80 other MPs.

Be unambiguous about sponsorship

Clause 9.10 of the Code states that material relating to medicines and their uses, whether promotional in nature or not, which is sponsored by a pharmaceutical company must clearly indicate that it has been sponsored by that company. The relevant supplementary information also requires that a declaration of sponsorship must be sufficiently prominent to ensure that readers of sponsored material are aware of it at the outset.

Companies must also ensure, however, that the wording of the declaration of sponsorship accurately reflects the company's involvement. For instance, it would be misleading to refer to an 'unrestricted educational grant' on a piece which has been initiated by a company and which consists almost wholly of data supplied by the company, even if the piece itself had been written by a third party. An arm's length arrangement should not be implied when in practice a company has been inextricably linked to the production of a piece. The same principle should be applied when declaring sponsorship of meetings.

Public reprimand for Roche

In a case where the Code of Practice Panel ruled no breach of the Code, Roche Products Limited has been publicly reprimanded by the Code of Practice Appeal Board for failing to provide accurate information to the Panel in its response to a complaint. The Appeal Board considered this matter to be of the utmost seriousness. In addition the Appeal Board has required an audit of Roche's procedures.

Full details can be found at page 3 of this issue of the Review in the report for Case AUTH/1819/4/06.

Don't allow a press release to become an advertisement!

Press releases about a medicine do not require prescribing information, although it is considered good practice to include a summary of product characteristics. Once a press release is issued, however, a company should have no control over the placement of any subsequent article and nor should it, or its agent, make any payment in relation to an article's publication. Where articles appear in the press should be at the publisher's discretion and articles should be printed wholly at the publisher's expense. If a company, or its agent, controls or in any way pays for the placement of an article about a product, then that article will be regarded as an advertisement for the product.

CODE OF PRACTICE TRAINING

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

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

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

Friday, 14 September
Monday, 15 October

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 Julie Gadsby for details (020 7747 1443 or email jgadsby@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.

MEDIA/DIRECTOR v ROCHE

Newspaper article about Herceptin

An article entitled 'The selling of a wonder drug' which appeared in the g2 supplement to The Guardian on 29 March criticized Roche's promotion of Herceptin (trastuzumab). In accordance with established practice the matter was taken up by the Director as a complaint under the Code.

The article alleged that Roche, or its public relations agency, tried to use a patient as part of its marketing strategy. It was also alleged that Roche organized a think tank for journalists paying each £250 for their time and giving them dinner in an expensive restaurant. The journalists were asked for their opinions on how best Roche could get stories into the media about its medicine for breast cancers that had spread to the bones.

The Panel noted that the article referred to a conversation between a named breast cancer patient and the spokeswoman from Roche who was reported as stating '… we're running a big campaign to promote Herceptin …' and 'Either we could find funding for Herceptin or … there would be fees for appearances [at seminars]'. Roche denied that it or its agency ever offered the patient a financial incentive to become involved or arranged access to treatment or asked her to promote Herceptin or speak at seminars. The Panel noted Roche's submission that its public relations agency had had a short conversation with the patient to ask her if she was interested in being involved in a disease awareness programme for breast cancer patients; the patient had already talked publicly about her disease. The Panel noted that the accounts differed significantly and there was little evidence. The Panel did not accept that the information before it was such as to show unequivocally that Roche had attempted to recruit the patient to promote Herceptin, that it had promoted Herceptin to her or that it had encouraged her such that she would ask her doctor to prescribe Herceptin. No breach of the Code was ruled.

The Panel noted that Roche had organised a media 'think tank' in March 2006. The Code did not prohibit such activity. Information made available directly or indirectly to the public about medicines such as via the press had to comply with the Code. The article stated that the journalists were asked how best the company could get stories in the media about its medicine for breast cancers that had spread to the bone. Roche stated that it was not the purpose of the meeting to get journalists to support a campaign for Herceptin. The aim was for the journalists to be used in an advisory capacity to talk about metastatic bone pain and breast cancer and cancer capacity within the NHS. It was to help Roche understand what journalists needed, what interested them and how to provide them with the right information. Roche did not provide information for publication. Confidentiality agreements were signed. [Note: Roche subsequently admitted that, due to an error, confidentiality agreements had not in fact been signed on this occasion.]

The Panel noted that again the accounts differed. Roche had not provided information to the journalists for publication, it had sought advice from them. On the basis of the information before it, the Panel considered that the activity did not constitute advertising prescription only medicines to the general public nor did it consider that information about medicines had been made available to the public either directly or indirectly. Thus the Panel ruled no breach of the Code.

With regard to the actual meeting the Panel noted that the supplementary information to the 2006 Code specifically stated that meetings for journalists had to comply with the Code. This was a requirement newly introduced into the 2006 Code. The relevant requirements of the 2003 Code only applied to hospitality provided to health professionals or appropriate administrative staff. The Panel noted that during the period 1 January 2006 to 30 April 2006, no activity could be regarded as being in breach of the 2006 Code if it failed to comply with its provisions only because of requirements newly introduced. Thus the Panel ruled no breach of the Code.

The Panel noted its rulings of no breach of the Code above and considered that, in consequence, there thus could, *inter alia*, be no breach of Clause 2 of the Code.

The journalist did not appeal but stated that contrary to Roche's submission, she had not been asked to sign a confidentiality agreement. Roche was asked to comment.

Roche stated that contrary to its response to the complaint, it had subsequently discovered that confidentiality agreements had not been signed by journalists. This only came to light because it investigated the point raised by the journalist in her letter to the Authority in which she commented upon, but did not appeal, the Panel's ruling.

The matter was referred to the Appeal Board which noted that the Code did not require confidentiality agreements to be signed. The Appeal Board was extremely concerned that Roche had stated that confidentiality agreements had been signed by journalists when this was not so; by stating that confidentiality agreements were signed when they were not, Roche had implied that by writing the article the journalist in question had breached a confidentiality agreement. The Appeal Board

considered this matter to be of the utmost seriousness. It was unacceptable to present assumptions as fact. It was of paramount importance that submissions to the Authority were checked for accuracy as the effectiveness of self regulation relied upon the integrity of the information provided by pharmaceutical companies. Roche had failed to provide accurate information to the Panel.

The Appeal Board decided in accordance with Paragraph 11.3 of the Constitution and Procedure that the Authority should carry out an audit of Roche's procedures in relation to the Code. In addition the Appeal Board decided to publicly reprimand Roche.

Upon receipt of the audit report the Appeal Board was concerned about arrangements for a meeting outside the UK and the management of the standard operating procedures. The Appeal Board decided that Roche should be reaudited in June/July 2007. The reaudit should include an update on the relationship between the UK and Head Office.

An article entitled 'The selling of a wonder drug' which appeared in the g2 supplement to The Guardian on 29 March criticized Roche's promotion of Herceptin (trastuzumab). In accordance with established practice the matter was taken up by the Director as a complaint under the Code.

COMPLAINT

The article alleged that Roche, or its public relations agency, tried to use a patient as part of its marketing strategy. It was also alleged that Roche organized a think tank for journalists paying each £250 for their time and giving them dinner in an expensive restaurant. The article also stated that the journalists were asked for their opinions on how best the company could get stories into the media about its medicine for breast cancers that had spread to the bones.

When writing to Roche, the Authority asked it to respond in relation to Clauses 2, 9.1, 20.1, and 20.2 of the 2003 edition of the Code.

RESPONSE

Roche stated that it had never set out to promote Herceptin to the public or encourage members of the public to request the medicine by name. The breast cancer patient named in the article had been approached by Roche's public relations agency shortly after her appearance in The Observer on 22 May 2005 in which she talked about her HER2 positive breast cancer. The patient was asked if she would be interested in becoming involved in a project that was being considered (but never actually completed) at the time called 'HER right to know'. This project was about a general disease awareness in women diagnosed with breast cancer ie awareness of specific diagnostic tests that should be conducted on their tumour.

In the interests of balance and integrity, the awareness would have involved all diagnostic tests that should be conducted, such as HER2, PR (progesterone receptor) and ER (estrogen receptor) and not an individual test or any specific treatment. As the conversation with the patient, when she said that she was not interested in taking part, was short, Roche's agency was unable to outline the full scope of this planned activity. No pressure was placed on the patient to participate in the project when she said she was not interested. Roche noted that 'HER right to know' had not developed, as the company considered that it had been superseded by a Department of Health (DoH) campaign to ensure that every breast cancer patient had access to a HER2 test.

Roche had decided to invite the patient to participate in the programme because of her previous willingness to appear in The Observer talking about her breast cancer and as a guest on television and radio discussion programmes. Roche stated that neither it nor its agency ever offered her a financial incentive to become involved, or arranged access to the treatment, or asked her to promote Herceptin or speak at seminars.

Roche stated that the telephone call had been misrepresented in the g2 article and the allegation that Roche was 'running a big campaign to promote Herceptin' was untrue. Indeed Roche's approach was more accurately represented in this article by the patient who stated that it had provided facts when asked but that Roche 'did not help her campaign at all', and 'they don't want any involvement with the campaign'.

In response to the issue of safety and efficacy that was discussed in the article, Herceptin was licensed in metastatic breast cancer in 2000. Herceptin was appropriate for the 1 in 5 breast cancer patients who had amplification of the HER2 gene.

Four independent studies had been conducted in the use of Herceptin in adjuvant disease. In April 2005 the National Cancer Institute announced the first in a series of results for Herceptin use in the adjuvant setting showing a 52% reduction in the risk of breast cancer relapse in HER2 positive patients. Three weeks later the Breast International Group made an unplanned presentation to the American Society of Clinical Oncology (ASCO) announcing the HERA data, from a pre-planned interim analysis. Data from these trials received an extremely strong response from ASCO attendees, who included mainly oncologists, but also members of UK patient organisations. Post ASCO, it was clear that the data had had a high impact globally, with oncologists around the world changing practice ahead of an official licence. The data were subsequently published as two separate papers and an editorial in the New England Journal of Medicine in October 2005. This issue of the journal included the two pivotal studies, and an editorial which included a comment that some patients might be cured. This was the most prestigious journal in the world, and none of the comments in it were influenced by Roche. It was this publicity and the extraordinary results of these

studies which had led to the unprecedented public and media awareness leading onto the issue of access to treatment. It was not due to a campaign organised by Roche as alleged.

In line with Clause 20.2 information about these new data and publications was communicated to the media via press releases, copies of which were provided. Roche had also sent these press releases to relevant patient organisations, so they had factual and accurate information to enable them to answer media calls that they received. Roche also answered further factual questions from these charities, such as questions about cost, on request.

Given the strength of the data, the strong clinical support for Herceptin, the patient group support for the medicine and the media environment (eg Kylie Minogue's recent breast cancer diagnosis) the news was widely covered. The newspapers continued their interest in the medicine and breast cancer. Over this time, Roche answered many media queries and responded to questions. On occasion the company had also had to send out separate press statements to clarify facts and correct mis-reporting. However Roche had also refused interviews with media and participation in TV programmes so as to avoid fuelling the media debate around Herceptin – especially at a time when Roche's regulatory submissions were being made.

Roche noted that the article in The Guardian referred to a survey to see how many of the women who were suitable were getting Herceptin which was then given to a cancer charity. The data to which the journalist referred was developed in 2002 following the NICE approval of Herceptin in metastatic disease. A robust algorithm was developed, and by using Roche sales data, implementation of NICE guidance across cancer networks was audited. Over a period of about 12 months leading experts, clinicians and finally patient organisations including the cancer charity were informed of this data within private discussions, and the outcomes discussed. There was major interest and eventually Roche agreed that the charity could use the data at its meeting in October 2003. Roche noted that it had provided the charity with the complete data set and support from its PR agency, but had had no direct involvement with the press activity that followed. It was clearly stated in the main body of the press release that the data had been supplied by Roche.

The NICE implementation audit was still widely used today. Roche updated the data approximately every 6 months and continued to share it with all interested parties. Given that implementation of NICE guidance was of major importance to many, the audit had been used or referred to in numerous external presentations, and cited as a model of best practice.

Roche noted that, further to the reference in The Guardian article to the funding of the charity, a letter from the charity in April 2006 clarified that, contrary to what had been reported, it received 7% of funding from pharmaceutical companies (of which only 0.26% was from Roche), and not the 31% that had been inaccurately reported.

Roche further noted that the article suggested that the company hoped to get support from patient groups, opinion leaders and journalists. In this regard Roche organised a media 'think tank' on 6 March 2006 but not with the purpose of getting journalists to support a campaign for Herceptin. The aim of the event was to bring about ten journalists together in an advisory capacity to talk about metastatic bone pain and cancer capacity within the NHS. The 'think tank' was devised to help Roche understand what journalists needed, what interested them and how to provide them with the right information. Roche reiterated that this advisory meeting was not to talk about Herceptin. It was usual for companies to consult a wide range of audiences to understand their knowledge of diseases and their impact on patients and society. When seeking strategic insight from these parties it was standard practice for confidentiality agreements to be signed, and for honoraria to be offered for participants' time, expertise and expenses. Roche submitted that the event complied with the Code.

Roche provided the invitation, agenda, and presentations from the evening. All the journalists signed confidentiality agreements which confirmed that Roche was not providing them with information that it wanted them to publish. [Note: Roche subsequently admitted that, due to an error, confidentiality agreements had not in fact been signed on this occasion.] In recognition of their time and professional expertise attendees were offered an honorarium of £200 (not £250 as reported in The Guardian). In all communication it was clearly stated that their attendance was requested for their counsel and expert contribution to the meeting discussions. The event was held in central London at a total cost per head of £50.

Invitations were sent to health correspondents at a range of media outlets. The author of the article at issue attended the meeting and the dinner which followed. She was invited because The Guardian was a respected newspaper, and like all newspapers guarded its independent reputation. In particular the author was known to take an investigative approach which Roche decided would give it a wider insight on the specific needs of a wide range of journalists and the media's needs. There was no intention to secure media coverage from the information provided at this event and indeed none to date had appeared which was not surprising in view of the confidentiality agreement. [Note: As indicated above Roche subsequently admitted that confidentiality agreements were not signed.]

Roche considered it conducted responsible activities that adhered to the Code, and did not compromise the impartiality and integrity of patient groups. Roche considered that its actions had not discredited the industry (Clause 2), that high standards had been maintained (Clause 9.1) and that it had not advertised a prescription only medicine to the general public (Clause 20.1). Similarly, information released by the company to the media was factual and presented in a balanced way; Roche had never sought to encourage members of the public to ask their doctor for a specific medicine (Clause 20.2).

PANEL RULING

The Panel noted that the published article referred to the conversation between a named breast cancer patient and the spokeswoman from Roche who was reported as stating '… we're running a big campaign to promote Herceptin …' and 'Either we could find funding for Herceptin or … there would be fees for appearances [at seminars]'. Roche denied that it or its agency ever offered the patient a financial incentive to become involved or arranged access to treatment or asked her to promote Herceptin or speak at seminars. The Panel noted Roche's submission that its public relations agency had contacted the patient to ask her if she was interested in being involved in a disease awareness programme for breast cancer patients; she had already talked publicly about her disease. Roche had submitted that the conversation was short. The Panel noted that the accounts differed significantly and there was little evidence. The Panel did not accept that the information before it was such as to show unequivocally that Roche had attempted to recruit the patient to promote Herceptin, that it had promoted Herceptin to her or that it had encouraged her such that she would ask her doctor to prescribe Herceptin. No breach of Clauses 20.1 and 20.2 was ruled.

The Panel noted that Roche had organised a media 'think tank' on 6 March 2006. The Panel noted that the Code did not prohibit pharmaceutical companies from consulting with journalists about the media or the placing of stories etc. Information made available directly or indirectly to the public about medicines such as via the press had to comply with the Code. The article stated that the journalists were asked how best the company could get stories in the media about its medicine for breast cancers that had spread to the bone. Roche stated that it was not the purpose of the meeting to get journalists to support a campaign for Herceptin. The aim was for the journalists to be used in an advisory capacity to talk about metastatic bone pain and breast cancer and cancer capacity within the NHS. It was to help Roche understand what journalists needed, what interested them and how to provide them with the right information. Roche did not provide information for publication. Confidentiality agreements were signed. [Note: Roche subsequently admitted that, due to an error, confidentiality agreements had not in fact been signed on this occasion.]

The Panel noted that again the accounts differed. Roche was not providing information to the journalists for publication, it was seeking advice from them. On the basis of the information before it, the Panel considered that the activity did not constitute advertising prescription only medicines to the general public nor did it consider that information about medicines had been made available to the public either directly or indirectly. Thus the Panel ruled no breach of Clauses 20.1 and 20.2.

With regard to the actual meeting the Panel noted that the supplementary information to Clause 20.2 of the 2006 Code specifically stated that meetings for journalists had to comply with Clause 19 of the Code. This was a requirement newly introduced into the 2006 Code. The requirements of Clause 19 in the 2003 Code only applied to hospitality provided to health professionals or appropriate administrative staff. The Panel noted that during the period 1 January 2006 to 30 April 2006, no activity could be regarded as being in breach of the 2006 Code if it failed to comply with its provisions only because of requirements newly introduced. Thus the Panel ruled no breach of Clause 19.1.

The Panel noted its rulings of no breach of the Code above and considered that, in consequence, there thus could be no breach of either Clause 9.1 or Clause 2.

The journalist did not appeal but subsequently noted that contrary to Roche's submission, she had not been asked to sign a confidentiality agreement. Roche was asked to comment and in a letter stated that contrary to its response to the complaint, the company had subsequently discovered that confidentiality agreements had not been signed by journalists. This only came to light because it investigated the point raised by the journalist in her letter to the Authority in which she commented upon, but did not appeal, the Panel's ruling.

The Authority referred the matter to the Appeal Board which decided to consider the matter formally.

APPEAL BOARD CONSIDERATION

The Appeal Board noted the submission from Roche that confidentiality agreements had not been signed on this occasion due to human error. Roche apologised for the error. Three similar 'think tanks' had already taken place where confidentiality agreements had been signed. Roche assumed that confidentiality agreements had therefore been signed at the meeting in question. The company had not verified this assumption before submitting its response to the complaint.

An external public relations (PR) agency had administered the meeting. Roche explained that typically at the outset of the meeting the PR agency would hand out confidentiality agreements to be signed which it would then collect and keep. At the three previous meetings a Roche employee had personally overseen the distribution and collection of these forms. This had not happened at the meeting at issue. Roche had a block contract with the PR agency which was then customised for each meeting by a project affirmation form. Roche could not confirm if that form specified the requirement for confidentiality agreements.

The Appeal Board noted that the Code did not require confidentiality agreements to be signed. However if a company was going to ask attendees to sign confidentiality agreements this should be made clear in advance so that invitees knew what was expected.

The Appeal Board was very concerned that by stating that confidentiality agreements were signed when they were not, Roche had implied that by writing the article

the journalist in question had breached a confidentiality agreement. It had subsequently come to light that this was not so. The Appeal Board considered this matter to be of the utmost seriousness. It was unacceptable to present assumptions as fact. It was of paramount importance that submissions to the Authority were checked for accuracy as the effectiveness of self regulation relied upon the integrity of the information provided by pharmaceutical companies. Roche had failed to provide accurate information to the Panel. This would have been easily avoided.

The Appeal Board decided in accordance with Paragraph 11.3 of the Constitution and Procedure to require an audit of Roche's procedures in relation to the Code to be carried out by the Authority. The audit would focus in particular upon Roche's relations with third parties, PR agencies, patient groups and its processes for responding to the Authority. In addition the Appeal Board publicly reprimanded Roche.

Upon receipt of the audit report the Appeal Board was concerned about arrangements for a meeting outside the UK and the management of the standard operating procedures. The Appeal Board decided that Roche should be reaudited in June/July 2007. The reaudit should include an update on the relationship between the UK and Head Office.

Proceedings commenced	**3 April 2006**
Case completed	**7 July 2006**
Report to the Appeal Board	**22 November 2006**

CASE AUTH/1857/6/06

CONSULTANT IN PUBLIC HEALTH MEDICINE v ROCHE

Activities regarding Herceptin

A consultant in public health medicine alleged that Roche, through various activities, had promoted Herceptin (trastuzumab) before the grant of its marketing authorization as an adjuvant treatment of HER2 positive, early breast cancer. For instance Roche's funding of the HER2 test for patients with early breast cancer had led to high expectations that patients with a positive result would be prescribed Herceptin. In that regard the complainant referred to an article which had been published on the website of the International Herald Tribune. When these expectations were unmet they had led to conflict which had undermined trust in the NHS as well as causing some criticism of Roche. The complainant further alleged that there was evidence to suggest that Roche had supported a patient group which pressurised public, political and media opinion in favour of Herceptin before it was licensed.

The complainant stated that Roche also appeared to be directly advertising to patients through its UK accessible HER2 website. On 27 April a headline in the patient section stated that, 'Study results show Herceptin reduces the risk of cancer coming back from women with early-stage HER2 positive breast cancer'. This was before a UK licence had been obtained and illustrated that promotion of the HER2 test was about encouraging patients to expect and demand Herceptin.

The complainant alleged that Roche had supported a patient group which had played a leading role in gaining media attention and pressurizing local and national politicians to fund Herceptin before its marketing authorization. Whilst Roche denied any direct funding, the patient group had reported by personal communication that it had been regularly directed to meeting key people and had supportive links with Roche or the public relation (PR) company that it employed. A Panorama programme, February 2006 reported that the leader of the patient group had visited Roche to give a motivational talk. There was also a summary of important links in a Guardian article, 'The selling of a wonder drug' March 2006, that suggested significant interference in the due processes by promoting Herceptin before marketing authorization.

The complainant stated that from The Guardian article there seemed to have been direct contact of a patient by Roche connected to the possible use of Herceptin. If this was true then it was worrying that Roche had obtained individual details and it was important to know where such information had come from. The complainant was also concerned that many patient groups had donations from pharmaceutical companies and some of those running Herceptin campaigns seemed to have encouraged patient contact when the medicine could not be obtained. One patient group site had a questionnaire on the delays in Herceptin availability, which asked, 'May we pass on your comments to the bodies listed above?' and it included Roche's name in the preamble.

The Panel noted that Herceptin had originally been authorized for the treatment of patients with metastatic breast cancer whose tumours overexpressed HER2. It was thus crucial to know a patient's HER2 status and the Panel noted the submission that establishing this at primary diagnosis was preferable to having to establish it once a patient had developed metastases. The DoH and a national cancer charity had both endorsed such action. Within that context the Panel did not consider that Roche's funding of HER2 testing encouraged patients with early breast cancer to expect that they would be treated with Herceptin. Roche's funding of the service would benefit patients and the NHS; there was no evidence that the service had been linked to the promotion of Herceptin. On the basis of the information before it the Panel considered that high standards had been maintained. No breach of the Code was ruled which was upheld on appeal by the complainant.

The Panel noted that a breast cancer patient, who was known to have received Herceptin therapy and who had set up a patient group, had been invited to talk to Roche staff about her experiences of living with cancer. In that regard the Panel did not consider it unreasonable for a company to invite a patient taking one of its medicines to talk to staff about their experiences. The Panel noted that the patient had only received her expenses and a bouquet of flowers; no monies were paid to the patient group. The Panel considered that any interaction between the group or one of its members and Roche was bound to attract attention. Nonetheless the Panel had no evidence to show that the interaction between the patient group leader and Roche had compromised the position of either. No breach of the Code was ruled which was upheld on appeal by the complainant.

The Panel noted that the patient group had been helped by a PR company, the contact between the two organisations had come about through an ex employee of Roche who worked for the PR company. Roche in the UK did not employ the PR company; it appeared that the only link with Roche and the PR company was through a global team based in Switzerland. The Panel thus considered that Roche had not influenced or supported the patient group through the PR company. No breach of the Code was ruled which was upheld on appeal by the complainant.

The Panel noted the complainant's reference to direct patient contact by Roche as reported in The Guardian. This matter had been considered in Case AUTH/1819/4/06. In that case, as in this case, the Panel noted Roche's submission that its PR agency had contacted a patient to ask her if she was interested in being involved in a breast cancer awareness programme for patients. The patient had already talked publicly about her disease. Roche had submitted that the conversation was short. In Case AUTH/1819/4/06 the Panel did not accept that the information before it was such as to show unequivocally that Roche had attempted to recruit the patient to promote Herceptin, that it had promoted Herceptin to her or had encouraged her such that she would ask her doctor to prescribe it. No breaches of the Code were ruled which were upheld in this case (Case AUTH/1857/6/06) upon appeal by the complainant.

The Panel noted that the article on the International Herald Tribune website had been prompted by an article in The Sun which had stated that Roche had promised money to train laboratory technicians to carry out HER2 testing. In response to a request, Roche had emailed the International Herald Tribune with brief details about its funding of HER2 testing. The Panel did not consider that the relatively short email, which was principally about Roche's funding of HER2 testing, promoted Herceptin. No breach of the Code was ruled which was upheld on appeal by the complainant.

With regard to Roche's HER2 website, the Panel noted that this was a site developed and produced by Roche in Switzerland. Roche in the UK had no input into it and nor did it promote the site in the UK. The Panel thus ruled no breach of the Code. Upon appeal by the complainant the Appeal Board noted from Roche that the website had been aimed at US citizens where promotion of prescription only medicines to the public was permitted. The Appeal Board noted that a Roche UK press release of 13 May 2005 included the website address under further information. The press release had originally been circulated, *inter alia*, to the lay media in the UK and remained available on the archive of the Roche UK website.

Taking all the circumstances into account and in particular noting that the website was aimed at members of the public in the US, the Appeal Board inferred that on the balance of probability at the relevant time, the site promoted prescription only medicines to the public. The Appeal Board thus considered that the reference in the press release of 13 May 2005, aimed at the lay UK media, to a website aimed at a lay US audience, amounted to promotion of a prescription only medicine to the public. The Appeal Board ruled a breach of the Code.

The Panel noted its rulings of no breach of the Code above and consequently ruled no breach of Clause 2 of the Code which was upheld on appeal by the complainant.

A consultant in public health medicine complained that Roche's funding of HER2 testing of patients and its involvement with a patient group had amounted to promotion of Herceptin (trastuzumab) before the grant of its marketing authorization as an adjuvant treatment of HER2 positive, early breast cancer.

COMPLAINT

The complainant alleged that Roche's funding of the HER2 test for patients with early breast cancer prior to Herceptin being granted a market authorization had led to high expectations that those patients with a positive result would benefit from Herceptin and therefore be prescribed it. When these expectations of early prescribing had been unmet they had led to conflict on a wide scale between patients, clinicians and primary care trusts (PCTs). Many PCTs had reasonably sought to await the detail of the licensing criteria in any marketing authorization before agreeing to fund the medicine for this new indication. As such these conflicts had undermined trust in the NHS as well as causing some criticism of the pharmaceutical company involved.

The complainant alleged that there was also evidence to suggest that Roche had sought to promote the role of a patient support group in pressurising public, political and media opinion in favour of the use of Herceptin before it was licensed.

The early promotion of Herceptin and the resultant pressures from patient groups and the media had directly led to political interference in the usual NHS processes for assessing and using a new medicine. This had caused considerable chaos and conflict. The advice on Herceptin use that came from the Department of Health (DoH) to the NHS was interpreted by many PCTs as a directive. This caused confusion in that it appeared to conflict with existing national policies on pharmaceutical licensing and on the role of the National Institute for Health and Clinical Excellence (NICE) in offering guidance on NHS priorities. The perception by many PCTs was that they would be taking unnecessary risks with patient safety by not waiting for the appropriate processes to take place.

The way that this issue arose had also caused some conflict between patients and PCTs with patients considering judicial review when their requests for funding were rejected. The adverse publicity that had been generated had also led to a misunderstanding by the wider community of what PCTs were trying to achieve with a consequent loss of confidence in the local NHS. It was obviously unhelpful to have different parts of the NHS in disagreement and a perception by some patients that the PCTs were acting perversely in not funding Herceptin before market authorization. A dangerous and irresponsible precedent had been set.

The complainant alleged that this unwarranted promotion of Herceptin had led to a fundamental clash between patients and clinicians on one side and

NHS commissioners on the other. Roche had played a part in this by unreasonably promoting Herceptin for early breast cancer before the medicine received its marketing authorization. The complainant noted from an article 'Roche step is positive signal on Herceptin' 9 December 2005 which appeared on the international Herald Tribune website (www.iht.com) that Roche had helped to fund the HER2 test for women with early breast cancer in the NHS and, with the consequent expectations of treatment for patients from a positive test, this could only be seen as promoting the use of the medicine before it received marketing authorization. Roche also appeared to be directly advertising to patients through its UK accessible HER2 website (www.her2status.com) (accessed on 27 April). It stated as a headline in the patient section that, 'Study results show Herceptin reduces the risk of cancer coming back from women with early-stage HER2 positive breast cancer'. This was before a UK licence had been obtained and again illustrated that promotion of the HER2 test was about encouraging patients to expect and demand Herceptin.

The complainant noted that the evidence that Roche had supported a patient group in its campaign for the funding of Herceptin was more circumstantial but nonetheless potentially serious and there appeared to be a case to answer. The patient group had played a leading role in gaining media attention and pressurizing local and national politicians to fund Herceptin before its marketing authorization. Whilst Roche had denied any direct funding, the patient group had reported by personal communication that it had been regularly directed to meeting key people and had supportive links with Roche or the public relation (PR) company that it employed. A Panorama programme of 5 February 2006 reported that the leader of the group had visited Roche to give a motivational talk. There was also a summary of important links in an article, 'The selling of a wonder drug' 29 March, in The Guardian that suggested significant interference in the due processes by promoting Herceptin before marketing authorization.

The complainant alleged that The Guardian article detailed the support for the patient group from a leading international PR and media company. Whilst the PR company stated that its support was 'pro bono', its UK section also had Roche as a client. It seemed naïve to expect people to believe that it was 'for the public good' when many might firstly disagree with the rationale behind the group's campaign in under cutting the process for drug licensing and secondly might also make a link with Roche through the PR company. Even if Roche had no direct involvement in encouraging the political campaigning of a key patient group so as to promote Herceptin, then it needed to be aware that it could be implicated in the PR chain through a company that it employed. Roche needed to be wary of this and to ensure that it exerted some contractual control over any PR or media support delivered through a third party so that it could not be accused of promoting a medicine before the grant of its marketing authorization.

The complainant further noted from The Guardian article that there seemed to have been direct contact of a patient by Roche connected to the possible use of Herceptin. If this was true then it was worrying that Roche had obtained individual details and it was important to know where such information had come from. The complainant was also concerned that many patient groups had donations from pharmaceutical companies and some of those running Herceptin campaigns seemed to have encouraged patient contact when the medicine could not be obtained. For example, one patient group site had a questionnaire on the delays in Herceptin availability, which asked, 'May we pass on your comments to the bodies listed above?' and it included Roche's name in the preamble. The complainant hoped that the link between the patient groups and the pharmaceutical companies did not extend to the misuse of this sort of information.

The complainant noted that Clauses 1.2, 20.3 and 20.4 should be considered in relation to the above.

When writing to Roche, the Authority asked it to respond, in addition to those clauses cited by the complainant, in relation to Clauses 2, 9.1, 20.1 and 20.4.

RESPONSE

Roche disagreed that its funding of HER2 testing services amounted to promoting Herceptin pre-licence variation.

Herceptin had been on the market in the UK since 2000, 'for the treatment of patients with metastatic breast cancer whose tumours overexpress HER2'. When Herceptin was introduced HER2 testing was not carried out routinely in the UK. Following discussions with leading oncologists and the NHS, Roche funded HER2 testing for the NHS using only three quality-assured reference laboratories for a period for 3 years. Roche submitted that this provision of a medical service was consistent with Clause 18.4.

In addition Roche submitted that it and most leading breast cancer specialists had consistently advised (since the launch of Herceptin for metastatic breast cancer) the early HER2 testing of patients at primary diagnosis. This advice pre-dated the advent of data supporting adjuvant use of Herceptin in 2005.

Roche submitted that the over expression of HER2 in breast cancer was associated with a worse prognosis. HER2 positivity halved patient survival compared with HER2 normal patients (Slamon et al, 1987). This alone justified testing at diagnosis in order to fully inform patients of the nature of their illness. There were also other reasons for HER2 testing at primary diagnosis unrelated to the use of Herceptin in early breast cancer - or indeed in metastatic breast cancer. Early testing (prospective testing) had a number of advantages over late, or retrospective testing.

- The prognostic value of HER2 status might

influence patients and clinicians in their choice of licensed treatments in the adjuvant setting.

- HER2 positive tumours responded better to aromatase inhibitors and anthracyclines in the adjuvant setting than HER2 negative tumours. Clinicians used this information in their decision making on treatments.

- Testing at the time of metastases was often associated with significant delays in establishing the HER2 status. If the test was delayed until advanced stages of breast cancer, which might be several years following initial diagnosis the patient's original tumour block needed to be retrieved from storage - where it might have been held for many years. Blocks could become damaged or lost, or the sample might degrade over time. Moreover, the costs incurred in retrieving the blocks meant that it could be more expensive to test at recurrence.

- Both audits and feedback from clinicians indicated that retrospective testing was often associated with delays, usually of several weeks. When dealing with aggressive metastatic cancer these delays might be clinically significant - with failure, or suboptimal treatment. The knowledge of HER2 status at the time of relapse allowed appropriate treatment to be instigated immediately. If HER2 status was unknown at the time of relapse the window of opportunity for optimal treatment could be missed.

- Early testing was recommended by some guidelines (Bilous *et al* 2003; St Gallen guidelines 2005).

HER2 positivity had clinical relevance beyond the use of Herceptin and early testing allowed better patient management. Similarly it was important that both the treating physician and the patient knew the HER2 status so that the necessary discussions about disease management could be held, and subsequent informed consent granted by the patient.

Roche submitted that despite the consensus that early testing was optimal, by September 2005 only 38% of breast cancer patients were HER2 tested at primary diagnosis. Subsequently, in October 2005 senior government officials issued statements that all early breast cancer patients should be tested for HER2 status at initial diagnosis. This was in part in response to the Herceptin adjuvant trial results but the decision was not influenced by Roche. At the time Roche did not sponsor HER2 testing. Many cancer networks were totally unprepared for the above statements and were unable to implement universal HER2 testing in a timely fashion. Indeed the complainant mentioned this ie 'the advice on Herceptin use that came from the DoH to the NHS was interpreted by many PCTs as a directive'. Moreover this part of the complaint seemed to be more about confusion relating to the NHS interpretation of guidance. There was no evidence that Roche had contributed to this or to the 'conflict between patients and PCTs leading to judicial reviews' which the complainant detailed.

Roche submitted that it was as a result of the statements on HER2 testing detailed above and subsequent discussions with the DoH that Roche agreed to support HER2 testing. Depending upon the network's particular need, Roche offered training for laboratory staff, help with development of local business case development, test kits, funding for laboratory staff for an agreed period or funding for tests to be done via a commercial laboratory. The company consulted and collaborated with the government throughout this process. Roche offered support to all cancer networks - currently 32 networks had an agreement with it. Some networks had not taken up the offer - so Roche's support was not universal.

Based on the above rationale, Roche therefore refuted the allegation that its support and funding for HER2 testing ahead of Herceptin's license extension in early breast cancer had promoted the medicine prior to the grant of its marketing authorization. Given the clinical rationale for determining HER2 status, together with the pre-existing licence of Herceptin in metastatic disease and the recommendation from the DoH that all women should be tested Roche considered its support of HER2 testing complied with Clause 18.4 of the Code, and benefited the NHS.

Roche submitted that it had never set out to promote Herceptin to the public or to encourage the public to request it by name. The publicity surrounding Herceptin in early breast cancer was due to the unprecedented results of the pivotal studies cancer presented at the American Society of Clinical Oncology (ASCO) in the Spring of 2005.

Four independent studies had been conducted in the use of Herceptin in adjuvant disease. In April 2005 the National Cancer Institute (NCI) announced the first in a series of results for Herceptin use in the adjuvant setting showing a 52% reduction in the risk of breast cancer relapse in HER2 positive patients. Three weeks later a European breast cancer specialist group made an unplanned presentation to the ASCO announcing the HERA data, from a pre-planned interim analysis. Data from these trials received an extremely strong response from ASCO attendees, which included mainly oncologists, but also members of UK patient organisations and media. Post ASCO, it was clear that the data had had a high impact globally, with oncologists around the world changing practice ahead of an official licence. The data were subsequently published as two separate papers and an editorial in the New England Journal of Medicine (NEJM) in October 2005. This issue of the journal included the two pivotal studies, and an editorial which included a comment that some patients might be cured. This was the most prestigious journal in the world, and it was not surprising that the results were highly influential. None of the comments in the NEJM were influenced by Roche.

Given the strength of the data, the strong clinical support for Herceptin, the patient group support for

the medicine and the media environment (eg Kylie Minogue's breast cancer diagnosis) the news was widely covered. The newspapers continued their interest in Herceptin and breast cancer. Over this time, Roche had answered many media queries. On occasion, there had also been the need to send out a press statement to clarify facts and correct mis-reporting. However Roche had also refused interviews with media and participation in television programmes such as Panorama so as to avoid fuelling the media debate around Herceptin - especially at a time when regulatory submissions were being made.

Roche submitted that given its portfolio of products it was not surprising that it had financially supported charities which helped people and their families affected by cancer. This financial support did not compromise the impartiality and integrity of patient groups and activities adhered to the Code.

Roche submitted that a full list of the charities that it supported was available on its website (www.rocheuk.com). Roche had also developed patient group contracts for activities in 2006 to ensure that patient groups retained their impartiality and integrity. This support was within the remit of the ABPI and was not done to influence such groups. Funding was associated with specific projects, such as sponsorship of an event. Roche did not influence the content or programmes of these events. Roche's support featured on any written material associated with these activities.

A number of charities had regularly commented to the media about Herceptin, many of whom had representatives independently present at the HERA data presentation at ASCO. Roche had not sought to influence such charities. In fact one of the most vocal advocates of the strength of the Herceptin data had received no funding from Roche. Another had been vocal in its criticism of Roche for what it perceived as the company's delay in applying for an adjuvant licence.

The complainant highlighted a questionnaire on a patient group website which asked 'May we pass your comments to the bodies listed above [inferring Roche]'. Roche did not know about the questionnaire until informed by the complainant, and it had never received any patient information from the patient group in this regard.

Roche submitted that following presentation of the HERA results at ASCO it had found out about a new patient organisation led by a metastatic breast cancer patient who had originally been treated with Herceptin through an expanded access programme. Roche was asked to fund this group, however given the nature of its campaign the company considered such funding wholly inappropriate for the reasons outlined in the complaint. Thus Roche had not funded this group.

Both The Guardian article and a Panorama programme (cited in the complaint), recognised that there was no evidence of Roche attempting to influence this patient group. As a responsible and ethical pharmaceutical company Roche had provided factual information to the patient organisation on request which was very much in line with requests from the other patient organisations. This included anticipated regulatory and NICE timelines and cost. Roche never encouraged the group to ignite a media campaign.

Roche noted that the complainant had stated that the patient group had been '…regularly directed to meeting key people and had supportive links with Roche'. Roche submitted that it had not directed this group to key people nor had it offered it any support or encouragement to obtain Herceptin prior to licence. The complainant referred to the Panorama programme which suggested that the leader of the group was invited to give a motivational talk at Roche. The patient was invited to speak to Roche international staff who worked in research and development (not sales and marketing) who were involved in the development of cancer medicines but not as a motivational talk; it had nothing to do with motivating sales of Herceptin. The title of her presentation was 'Breast Cancer - a patient's perspective' and as suggested by the title was about her experience of living with the disease; her presentation was not about Herceptin, though she referred to this once when discussing her overall treatment. Roche had not sponsored or in any other way encouraged the patient to speak to any other groups.

In response to a request for further information Roche explained that there were two separate organizations based at its head office site; Roche Pharma Development (PD) which was a global function that dealt with the development of new medicines and regulatory affairs on an international basis and Roche Products Ltd which was the UK marketing affiliate. Staff in PD organised a series of seminars on general interest topics that were not necessarily work-related.

The invitation to talk to the group was offered to the leader of the patient group who was known to the company as a person living with breast cancer and who had been treated with Herceptin. She had subsequently set up the patient group.

The leader of the patient group spoke about her illness and sequence of treatment. No honorarium was paid but she was presented with a bouquet. Her travelling and accommodation expenses were paid (details were provided).

In summary this was not an official company meeting organised by the UK affiliate of Roche for motivational purposes but a meeting organised by a group of employees of PD who arranged occasional seminars for staff on topics of interest.

With regard to the suggested a link between Roche, a PR agency and the patient group referred to in The Guardian, the facts were that an ex-employee of Roche currently working at the PR agency, offered pro-bono media support to the group. This ex-

employee knew of the patient group leader from her employment at Roche. However the offer from the PR agency was not funded or driven by Roche in any way and was a matter for the PR agency. The complainant stated that the PR agency had Roche as a client thus implying Roche must have been involved.

Roche submitted that Roche UK did not employ the PR agency. However a global team, based in Switzerland, employed the PR agency in 2005. Given that Roche UK did not work with the PR agency, and that the PR company's decision to offer unpaid service to the patient group was its decision and outside the control of Roche, it did not agree that 'Roche should be implicated in the PR chain of events', and that it promoted Herceptin to the general public.

In conclusion, Roche noted that patient groups were there to service and support their patients and members that they represented and whilst this would encompass a whole series of important initiatives, access to medicines that had the potential to prolong and save lives had been, and would continue to be an important area for patient groups to engage.

Roche noted that the complainant had referred to The Guardian article in which it was alleged that Roche had approached an individual patient and encouraged her to 'promote Herceptin'. Roche confirmed that the patient was approached by its PR agency shortly after she had appeared in The Observer talking about her HER2 positive breast cancer. The patient was telephoned to see if she would be interested in becoming involved in a general breast cancer awareness project. Roche submitted that in the interests of balance and integrity, the project would have provided information on all diagnostic tests that should be conducted, such as HER2, progesterone receptor and oestrogen receptor and not any individual test or any specific treatment. Due to the brevity of the conversation with the patient when she said that she was not interested in taking part, the PR agency was unable to outline the full scope of this planned activity. No pressure was placed on the patient to participate in the project when she said she wasn't interested. In the end the project was not developed as Roche considered that it had been superseded by the DoH's announcement on HER2 testing discussed above.

Roche submitted that the patient had been invited to participate in this project because of her previous willingness to appear in The Observer talking about her breast cancer and as a guest on television and radio discussion programmes. At no point did Roche or its PR agency offer a financial incentive to become involved, offer to arrange access to the treatment, ask her to promote Herceptin or speak at seminars.

Roche considered that the telephone call had been misrepresented in the newspaper article and it further objected to the untrue allegation that it was 'running a big campaign to promote Herceptin'. Indeed Roche's approach was more accurately represented in this article by the patient who stated that it had provided facts when asked but was quoted as saying Roche 'did not help her campaign at all' and 'they don't' want any involvement with the campaign'.

Roche noted that the allegations made in The Guardian had been reviewed by the Medicines and Healthcare products Regulatory Agency and no breach of Regulation 7 of the Advertising Regulations was found.

In summary Roche submitted that it had acted responsibly, and had not sought to promote Herceptin to the general public or threaten the integrity of the pharmaceutical industry.

Roche submitted that other activity outside of its control had been legal action of patients seeking to gain access to the treatment; the solicitor acting on behalf of these individuals had employed the service of a media relations agency. This again was without Roche's knowledge and there had been no communication between this communications agency, Roche and any other communications agency acting on its behalf. In fact the first that Roche knew about the involvement was when a journalist contacted the communications department at Roche and said they had received a call from its public relations agency.

In summary Roche submitted that the unprecedented interest in Herceptin was due to:

- The strength of the data presented at ASCO and published in the NEJM which showed that this class of medicines was dramatically changing the course of breast cancer.
- The strong clinical support for Herceptin from breast cancer specialists, which was almost universal.
- The media environment (eg Kylie Minogue's breast cancer diagnosis).
- The patient group support for the medicine (as deemed by their medical advisory committees).
- Patient legal action and solicitor-driven publicity.
- Individual patient campaigners.

Roche submitted that the significant interest in Herceptin was not due to a campaign organised by Roche and it had not sought to promote Herceptin to the general public. Conversely Roche had tried to maintain a degree of fairness, balance and accuracy in the reporting of Herceptin and to manage expectations about the treatment. Due to a series of events not in the control of Roche, its communications department had answered a lot of media enquires relating to Herceptin.

Roche hoped the above helped explain how its activities were developed and implemented. Roche considered its activities to be responsible, and within the letter and the spirit of the Code, and had not

compromised the impartiality and integrity of patient groups. Roche did not consider it had promoted Herceptin (Clause 1.2) or that its actions had discredited the industry (Clause 2), and that it maintained high standards (Clause 9.1). Roche had not advertised a prescription medicine to the public (Clause 20.1). Roche had never sought to encourage members of the public to ask their doctors for a specific medicine (Clause 20.2). Roche had supported patient groups, in line with the Code, to ensure impartiality and integrity (Clause 20.3). Roche had made factual information about Herceptin registration, NICE guidelines and cost, available to patient groups who had requested such. Finally, Roche had never advised members of the public on personal medical matters (Clause 20.4).

In response to a further request for more information Roche noted that the complainant had referred to an article that had appeared on the International Herald Tribune's website detailing Roche's provision of £1.5million HER2 testing funding support to the NHS. The International Herald Tribune had asked Roche for details of this financial support following the publication of an article in The Sun newspaper which gave brief details of an agreement between Roche and the DoH for Roche to provide financial support to help the NHS cope with an expected surge in the demand for HER2 testing. Roche had had no involvement with the article in The Sun.

The International Herald Tribune asked Roche why, as this was potentially a 'good news' story, had Roche not released details of it to the media. Roche replied that it had decided not to release these details to the general media, due to concern it would ignite media interest in Herceptin, prior to a decision on licence. As the information had already appeared in The Sun and the International Herald Tribune had specifically requested them, the details were sent in a non-promotional email that reiterated the company's original decision not to release details of this funding commitment. The article which was balanced in tone appeared the following week.

Roche also noted that the complainant had referred to a website which discussed the importance of HER2 testing. This website was developed and produced by Roche group headquarters in Switzerland. Roche UK has had no input into the website is nor did it promote it in the UK. Clause 21.2 stated 'Information or promotional material about medicines … which is placed on the internet outside of the UK will be regarded as coming within the scope of the Code if it was placed there by a UK company or an affiliate of a UK company or at the instigation or with the authority of such a company'. Given that Roche was a Swiss company and that Roche UK had had no involvement in the development or content of the site, nor did it use the web address in promotional materials or promote it within the UK, the company considered the complainant's reference to this site was outside the scope of the Code and the responsibility of Roche UK. In the section of the website that detailed patient support groups Roche noted that a range of such organisations were listed from a range of countries. The inclusion of hyperlinks to UK-based patient support information appeared to be in the context of providing the most appropriate support and information to patients, some of which happened to originate from UK charity sites and certainly did not indicate that Roche in the UK intended UK patients to visit this site.

PANEL RULING

The Panel noted that Herceptin had originally been authorized for the treatment of patients with metastatic breast cancer whose tumours overexpressed HER2. It was thus crucial that a patient's HER2 status was known and the Panel noted the submission that establishing this at primary diagnosis was preferable to having to establish it once a patient had developed metastases. The DoH and a national cancer charity had both endorsed such action. Within that context the Panel did not consider that Roche's funding of HER2 testing encouraged patients with early breast cancer to expect that they would be treated with Herceptin. Roche's funding of the service would benefit patients and the NHS; there was no evidence that the service had been linked to the promotion of Herceptin. On the basis of the information before it the Panel considered that high standards had been maintained. No breach of Clause 9.1 was ruled.

The Panel noted that a breast cancer patient who had set up a patient support group had been invited to talk to Roche staff about her experiences of living with cancer, she was known to have received Herceptin therapy. In that regard the Panel did not consider it unreasonable for a company to invite a patient taking one of its medicines to talk to staff about their experiences. The Panel noted that the patient group leader had not received any payment as such - only her expenses and a bouquet of flowers; no monies had been paid to the patient group. The Panel considered that any interaction between the group or one of its members and Roche was bound to attract attention. Nonetheless the Panel had no evidence to show that the interaction between the patient group leader and Roche had compromised the position of either. No breach of Clause 9.1 was ruled.

The Panel noted that the patient group had received some help from a PR company, the contact between the two organisations had come about through an ex employee of Roche who worked for the PR agency. Roche in the UK did not employ the PR agency; it appeared that the only link with Roche and the PR agency was through a global team based in Switzerland. The Panel thus considered that Roche had not influenced or supported the patient group through the PR agency. No breach of Clause 9.1 was ruled.

The Panel noted the complainant's reference to direct patient contact by Roche as reported in The Guardian. This matter had been considered in Case AUTH/1819/4/06. In that case, as in this case, the Panel noted Roche's submission that its public

relations agency had contacted a professor to ask her if she was interested in being involved in a disease awareness programme for breast cancer patients. The professor had already talked publicly about her disease. Roche had submitted that the conversation was short. In Case AUTH/1819/4/06 the Panel did not accept that the information before it was such as to show unequivocally that Roche had attempted to recruit the professor to promote Herceptin, that it had promoted Herceptin to her or that it had encouraged her such that she would ask her doctor to prescribe Herceptin. No breaches of Clauses 20.1 and 20.2 were ruled.

The Panel noted that Roche had not known about the patient questionnaire on the patient group website until it had received this complaint. Given the company's lack of involvement the Director determined that there was no *prima facie* case to answer.

The Panel noted that the article which had appeared on the International Herald Tribune website had been prompted, in the first instance, by an article in The Sun which had stated that Roche had promised more than £1million to train laboratory technicians to carry out HER2 testing. In response to a request from a correspondent on the International Herald Tribune, Roche had provided brief details about its funding of HER2 testing. The Panel did not consider that the relatively short email from Roche to the correspondent promoted Herceptin. The email was principally about Roche's funding of HER2 testing not about Herceptin. No breach of Clause 20.1 was ruled.

With regard to the website HER2status.com, the Panel noted that this was a site developed and produced by Roche in Switzerland. Roche in the UK had no input into the site and nor did it promote the site in the UK. The Panel thus ruled no breach of Clause 20.1.

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

APPEAL BY THE COMPLAINANT

The complainant noted that he had complained about the promotion of Herceptin for its use in early breast cancer, before it had been given the appropriate marketing authorization to try and make pharmaceutical companies aware that it was unacceptable to create a climate where commissioners of healthcare were put under severe pressure to act against major policies. This pressure with Herceptin came from the public, patients, press and clinicians, and was focussed through the politicians such that a number of commissioners felt obliged to undermine the law regarding market authorization and circumvent the national policy on using NICE to advise on NHS funding. The complainant wanted to ensure that NHS commissioners had the appropriate time to consider the clinical evidence, safety and cost effectiveness of a new treatment without taking undue risks with patients' safety or NHS funds. The complaint was not about the use of Herceptin for metastatic breast cancer.

The complainant alleged that Roche's timing of financial support for HER2 testing through the NHS in 2005 belied the arguments about the value of the test as a prognostic indicator. Whilst the HER2 test might have value as a prognostic indicator for a clinician this was not the business of Roche. Press releases from Roche clearly related the HER2 test to the use of Herceptin for patients . The press release from Roche dated 13 May 2005, which quoted a leading clinician endorsed the obvious link between the HER2 test and Herceptin: 'This is a very important advance for patients with so-called HER2 positive breast cancer, which is generally more aggressive. We now need to make plans quickly for measuring the HER2 status of all breast cancer patients at diagnosis, to determine everyone who could benefit from such treatment.'

The complainant alleged that the press release continued to emphasise the link between the diagnostic test and treatment through to the notes section. Whilst early testing might be useful, the context at this time was that the research was not published in a peer-reviewed journal and Herceptin was a year away from authorization in the UK. As such the encouragement to use the test prejudged the marketing authorization and was highly likely to lead patients, who might have had the test following early breast cancer, to expect that they should receive the medicine. This in turn undermined the independence of the licensing authority, the EMEA, as well as the role of NICE.

The DoH endorsed the funding of early HER2 testing following the support of senior government officials. This action was seen as misguided by many as it caused a conflict between national policies (the Medicines Act and NICE authorization) and subsequent chaos amongst NHS funding authorities (PCTs in England and local health boards in Wales). One senior government official, whilst encouraging the funding of Herceptin, acknowledged this legal conflict in a speech on 25 October 2005 without clarifying how this could be resolved by PCTs. This political action could be seen as promoting the use of a medicine before its market authorization although where that sat with individuals in terms of the Medicines Act was not clear. The DoH letter of 17 October 2005 linked HER2 testing with the assumption that Herceptin was to be licensed and to be given NICE approval. However, this unprecented political action could not be interpreted as an invitation for Roche to participate and become part of the unwarranted promotion of Herceptin at this early stage.

The complainant provided copies of letters and emails relating to funding by Roche of the HER2 test to a local cancer network. A letter from Roche was very specific in its expectations and from comments in the emails its representative was seen as pushing the commissioning clinician into an arrangement she was unhappy with.

Part of this was an unease with the fact that Roche wanted to be given the data from the HER2 test results. Why Roche needed this data if it was only supporting a DoH initiative was unclear and could only lead to the inference that it was for commercial reasons related to the marketing of the Herceptin.

As regards Clause 18.4 of the Code the complainant presumed that the provision of patient services to the NHS was only intended to relate to general support and not to the funding of services such as the HER2 test that promoted a specific product particularly when the product was not licensed. As stated before, the timing and nature of this sponsorship suggested that it was largely intended to raise the pressure for Herceptin to be funded in advance of marketing authorization and also to make that authorization appear inevitable.

The complainant noted the points raised by Roche about the ASCO conference and the HERA trial. Many healthcare commissioners saw this conference as an important place for the early promotion and marketing of pharmaceuticals that had yet to be fully assessed and given marketing authorization.

The complainant noted that the ASCO conference in late spring appeared to be well orchestrated in the way that it promoted new treatments in a commercial way. Immediately preceding the 2005 conference Roche issued an investor update, dated 28 April 2005, on its worldwide website in which it announced the interim analysis of the HERA trial. In this case the reference by Roche in its response to 'an unplanned presentation' was misleading. The ASCO conference had specific sessions for 'late-breaking results' and a publicity machine that would make the most of any announcements on interim results. There were well-recognised problems with presentations at conferences that announced incomplete analyses (neither peer-reviewed in a journal nor validated for presentation for marketing authorization). These problems, often of undue optimism based on incomplete results (Montori *et al* 2005), were likely to be compounded by the attendance at conferences, such as ASCO, of the media, UK patient organisations and the public. Clearly it was not just a conference for the exchange of information between clinicians and researchers.

The complainant alleged that the group that had made the 'unplanned announcement' had collaborated with Roche in the HERA trial (Roche UK press release 13 May 2005). From the complainant's knowledge of research trials this usually meant that the sponsoring pharmaceutical company would have a well-specified contract with the trial participants and therefore some control over how, when and where the results were presented. Roche also had some sponsorship of ASCO and it was important to know if this included direct sponsorship of the conference where its trial results were presented.

The complainant alleged that there was no disputing the widespread interest and media environment around Herceptin at this time. The reasons for this were not as straightforward as Roche suggested. The expectations from new research could be given a large boost by the one-sided publicity and marketing that could be engineered by careful targeting at an ASCO conference. The wider view that emerged from the evidence and the media impact was that an astute pharmaceutical company such as Roche could set its marketing campaign alight at ASCO.

Searching Roche UK's media release archive for Herceptin brought up one news item. This was the press release dated 13 May 2005 referred to above which acknowledged the role of the influential ASCO conference. There were also a number of press releases on Roche's international website that were listed as media or investor updates at around the same time. Whilst these could be seen to be general marketing for a large multinational company, issuing such a specific press release in the UK was marketing that was inappropriate under the Code.

The complainant alleged that there was also an issue around the Herceptin research data, and the interpretation of the data by the public and breast cancer patients, that in its marketing was misleading and inappropriate. This point emphasised again the context, which led to the political pressure and the consequent pressure on PCTs. There were a number of examples where patients and even an MP thought that being given Herceptin allowed patients to survive and being denied it meant death. It was not surprising that patients and a lot of the public viewed PCTs as perverse in not funding Herceptin at an early stage. In reality the prognosis for early breast cancer was relatively good and was one of the reasons that Herceptin had a number needed to treat (NNT) of the order of 16 to allow one extra patient to survive at four years. Much of the data was presented as relative risk information rather than as the more meaningful absolute risk information and often the figure of a 50% decrease in disease recurrence was used without a clear explanation of the survival data. Given this issue it would be useful to have more of the press statements that Roche referred to in its response to the complaint as being helpful to clarify facts and correct misreporting.

The complainant alleged that Roche had acknowledged the role that the ASCO conference played but completely understated its part in helping to set up this role and allowing the subsequent patient, media and political campaigns to gather force so as to pressurise healthcare funders.

The complainant noted that the patient group, founded by the breast cancer patient who had subsequently given a talk to Roche personnel, had played an unprecedented role in raising the profile of Herceptin in the UK. For this reason and those given in more detail below it was important to see more evidence from Roche regarding the link between Roche in Switzerland and the PR agency which had helped the patient group.

The complainant alleged that the patient group had gained widespread local and national publicity and as

a consequence had directly influenced local and national politicians who in turn were unhappy about the adverse newspaper comment that it generated for the Government. This sequence of events was fundamental to the national polarisation of views around Herceptin and the conflict that occurred between PCTs and the DoH, as well as seeing conflict between PCTs and their patients on a scale that had not occurred before. This explanation was important not just to understand the importance of this patient group but also to try and understand how it happened.

The patient group was founded by a breast cancer patient, who had also set up a registered eponymous breast cancer charity with local aims and an income of around £8,000 in 2004. The complainant submitted that it did not seem rational to outside observers that such a small group should be courted by one of the top ten international public relations company, which was linked with the sixth largest pharmaceutical company in the world, without there being some longer term aim. Given that Roche UK had refused to fund this group, it seemed dangerous territory for a subsidiary company in the same building to invite the patient group leader to give a talk when that patient group was not a charity but had specific aims to widen the use of Herceptin. The patient group was not set up after the leader of it talked to Roche staff in December 2005; it was already well established by the middle of 2005.

The complainant suspected that Roche was right in stating that there was no evidence of it attempting to influence this patient group. However, given the uncertainties that were raised about possible links it was important to see evidence relating to the links between the Roche global team and the PR agency. The importance of this was that the PR agency had a reputation for fostering conflicts of interest. A disconcerting example was that a president from the PR agency had lead a conference session on guerrilla media tactics – generating buzz on media radar without news. This was a remarkably apt description of how the PR agency affected the campaign of the patient group. Many would not see this as pro-bono activity when it actually cut across the public interest by undermining the Medicines Act. It was important to have the details of the Roche/PR agency relationship clarified.

The complainant noted that Roche stated that Roche UK had no involvement in the development or content of the HER2 testing website. At the time it was accessed and before UK market authorization had occurred this website carried a news update box on the patients' home page stating: 'Interim analyses of three major Herceptin studies show that Herceptin has the potential to significantly increase the length of time after treatment during which no disease is found (disease-free survival) for women with early-stage HER2 positive breast cancer'. The complainant submitted that it was disingenuous to claim that as a subsidiary company there was no responsibility at Roche in Switzerland or in the UK for the role that this website could play. Other parts of Roche should know well that their activities might impact on the legal position of a company such as Roche UK and should be cautious in their role where they might be seen to be promoting a medicine ahead of its market authorization.

The complainant submitted that Roche UK was well aware of this website. The news article on Roche UK's website under the media release archive section (dated 13 May 2005) listed the website address at the end of a section headed, 'About breast cancer and Herceptin'. This contradicted Roche UK's statement that it did not use the web address so as to promote it within the UK and negated the disclaimer on the website. It also suggested that Roche UK was well informed about the website and was in close communication with its Swiss headquarters. Some of the information contained in an investor update from Roche International's website (dated 28 April 2005) was identical to some of that in the Roche UK press release. This update also included the website address, www.HER2status.com. By its very nature a press release was about publicity. A complaint with some parallels although obviously differing in the details was upheld as a breach of the Code at appeal (Case AUTH/1801/2/06).

In summary, the complainant submitted that the unprecented interest in Herceptin that Roche itself highlighted was initiated at the ASCO conference and supported in a number of ways by both Roche International and Roche UK.

The complainant alleged that it was difficult to separate the worldwide campaign from the initiatives in the UK as the evidence linked both. To deny that there were close links between the headquarters and its subsidiary and that their responsibilities were interrelated would undermine the Medicines Act. The promotion of the HER2 test and, more importantly, the way that the test was funded in advance of market authorization so as to raise the expectations of patients that they would receive Herceptin were both evidence that Roche UK sought to prematurely promote the funding and use of the medicine.

The complainant alleged that there was much other evidence as discussed above that gave a context to the unprecedented interest in Herceptin. The number of factors that Roche described in its response were set in train at the ASCO conference and fostered by Roche. Healthcare commissioners in the UK needed to work well with the pharmaceutical industry in the interests of the patients and the wider public. If the Herceptin scenario was not to be repeated then the Appeal Board must consider seriously the documented breaches of the Code.

COMMENTS FROM ROCHE

Roche reiterated that HER2 status was a key prognostic indicator, and that it initially supported HER2 testing prior to the adjuvant data becoming available. In addition to the details previously provided, a group of experts had recently published

new guidance on risk assessment in early breast cancer which demonstrated the importance of HER2 status in defining risk and in deciding whether treatment with chemotherapy was appropriate. The guidelines considered that no patient with a HER2 positive tumour could be classified as 'low risk' (Goldhirsch *et al* 2006).

Roche submitted that patients should know the nature and prognosis of their disease and that clinicians should take informed decisions regarding their management, particularly as approximately 77% of patients were HER2 negative and did not require HER2 targeted therapy such as Herceptin. These patients had less aggressive tumours and a better prognosis.

Similarly, whilst Roche acknowledged the complainant was concerned about Herceptin in early breast cancer, it was important to note that Herceptin had been licensed for 6 years in metastatic disease. As previously stated, 5 years after Herceptin was licensed in metastatic disease, only 38% of breast cancer patients were HER2 tested at primary diagnosis. This meant that in September 2005, 62% of patients did not know their HER2 status on diagnosis, clearly not optimal for their disease management. Therefore the rationale for HER2 testing was just as important for metastatic patients as it was for adjuvant patients.

Roche submitted that its financial support of HER2 testing services was in response to Government statements that all breast cancer patients should be HER2 tested on initial diagnosis. The complainant himself had noted that the DoH had endorsed the funding of HER2 testing and cancer networks had been encouraged to liaise with Roche regarding HER2 testing. Given Roche's support and extensive knowledge about HER2 testing services from its experiences in metastatic disease it would have been surprising if it had not been involved in an initiative aimed at ensuring that all breast cancer patients were HER2 tested on diagnosis.

Roche considered that funding HER2 testing that had prognostic importance, in response to ministerial and NHS statements, was not promotion of Herceptin as made clear previously and did not undermine the independence of the licensing authority, the EMEA or NICE and complied with Clause 18.4 of the Code.

Roche noted that the complainant referred to a quote from a leading clinician in its press release of 13 May 2005. This media release was issued by Roche UK in relation to the publication of the HERA trial at ASCO; the principal UK investigator stated 'This is an important advance for patients with so-called HER2 positive breast cancer, which is generally more aggressive. We now need to make plans quickly for measuring the HER2 status of all breast cancer patients at diagnosis, to determine everyone who could benefit from such treatment'. The main body of the press release also highlighted that 'the infrastructure needs to be in place to cope with an increased demand for HER2 testing when Herceptin becomes more widely used for early stage breast cancer'.

Roche submitted that the interest in Herceptin highlighted the low level of HER2 testing in the UK, in September 2005 only 38% of patients were being tested. Roche submitted that it had not breached the Code in highlighting that HER2 testing services needed to be improved and did not agree that these statements constituted promotion of its medicine prior to marketing authorization. Also the decision to encourage HER2 testing at initial diagnosis was taken by the DoH as noted above.

Roche had reviewed the correspondence provided by the complainant relating to funding by Roche of the HER2 test for a local cancer network. With regard to the company's expectations Roche submitted that it was not good practice to simply award grants without a specific agreement in place, and to ensure that funding was being used in accordance with the Code. Roche was willing to fund the specific needs of each network in setting up an efficient HER2 testing service; it thus specified very clearly exactly what the funding was in order to avoid any subsequent issues.

With regard to wanting data from the HER2 test results, Roche explained that before embarking upon this project it undertook to tell the Cancer Action Team at the DoH how many tests were being conducted and the numbers that were HER2 positive in each cancer network. These data contained no individual patient information and were not related to commercial activity. Roche had discussed with the National External Quality Assessment Service issues about handing over this information to help it with quality assessments. Confidentiality was clearly laid out in the initial agreement.

Roche understood that the Cancer Action Team nominated a HER2 lead in networks following the initial DoH announcement, and this person would be the Roche contact for service development. The majority of networks met with Roche fairly early in the process (before the end of 2005) and it was able to develop a tailored contract in collaboration with their HER2 lead. Roche put together a draft contract as a basis for discussion, and mailed it via its healthcare management team, to the HER2 lead as a starting point in discussion. The enclosure provided by the complainant suggested this approach was made on 28 February 2006, with a follow-up email three months later (25 May 2006). The clinician involved had every opportunity to comment on the agreement, and any follow-up from Roche would have been in terms of obtaining a response to the offer.

Roche submitted that given the clinical rationale for determining HER2 status, together with the pre-existing licence of Herceptin in metastatic disease, the fact that only 38% of breast cancer patients were HER2 tested on diagnosis in September 2005 and the recommendation from the DoH that all women should be tested, it considered that its support of HER2 testing complied with Clause 18.4 of the Code, and benefited the NHS. This service did not constitute promotion of a specific product, nor pre-marketing of

that product. Roche disagreed that its support of HER2 testing raised the pressure for Herceptin to be funded in advance of licence.

Roche submitted that ASCO was a large, clinical oncology society which by its very definition was integral to the treatment of cancer. An independent scientific committee evaluated and agreed the scientific content and the format of the annual conference. Pharmaceutical companies provided money to support logistics and for exhibition space at the conference, however this was not related to scientific content. The scientific committee of ASCO selected data for presentation (either oral or poster) and information that was publicised from the conference; the industry did not influence the scientific content or ASCO-generated publicity although companies might choose to issue their own press releases on data relevant to their medicines. If the complainant was concerned about the way ASCO was organised then he should contact the conference organisers directly.

Roche submitted that the group that had made the unplanned announcement about the HERA trial at ASCO was a multinational group of independent researchers who conducted clinical trials on new investigational medicines, not exclusive to Roche. Roche Switzerland led the contact with the group and funded it to run the HERA trial. The steering committee of the group also decided on progress and procedure of its trials, including when data was published. This was overseen by an independent data review committee.

Roche understood that the clinical results from two other studies of Herceptin in adjuvant breast cancer run by the US National Cancer Institute became available after the deadline for 'latebreaker' abstracts. The ASCO scientific committee realising the importance of this newly available data decided to organise a special 'unplanned' session reviewing advances in breast cancer. This session included the two US studies, HERA, and a study involving another unlicensed treatment, bevacizumab. This type of special session had never been instituted before which underscored Roche's contention that the results of these studies had driven the worldwide interest in Herceptin treatment.

Roche submitted that the investor update the complainant referred to related to an announcement made from its headquarters in Switzerland (Basel 28 April 2005) which did not include the actual data itself from HERA, but confirmed that interim data met its primary endpoint and showed improved disease free survival in women. Companies of the Roche Group, had a financial obligation, to some extent even a legal obligation, to inform investors of new information that might impact share price.

Roche submitted that the widespread public interest in Herceptin was multifactorial. The strength of the data, the strong clinical support for Herceptin, the patient group interest and the media environment (eg Kylie Minogue's breast cancer diagnosis during the ASCO congress) contributed to the news being widely covered. Roche had distributed the press release mentioned by the complainant dated 13 May in the UK from ASCO, which was in line with Clause 20.2 of the Code. Supplementary information to Clause 20.2 stated 'This clause allows for provision of non-promotional information about prescription only medicines to the public either in response to a direct enquiry from an individual, including enquiries by journalists, or by dissemination of such information via press conferences, press announcements, television and radio reports, public relations activities and the like'. Roche therefore disagreed that distribution of a press release based on the HERA results presented at ASCO was inappropriate under the Code.

Roche submitted that the press release from ASCO stated the data presented and made it clear that Herceptin reduced the risk of breast cancer returning by 46%. Roche agreed that some of the media reporting misrepresented the data, which was why it distributed a fact sheet in February 2006 and thereafter to counteract the misinformation circulating. Roche also disagreed with the complainant's statement that 'in reality the prognosis for early breast cancer is relatively good…'. Whilst that might be so for HER2 negative patients, it was not the case for HER2 positive patients (Goldhirsch *et al* and Slamon *et al*).

Turning to the issue of the patient group, Roche submitted that the PR agency was appointed by a team in Basel to organise one internal meeting. This had nothing to do with breast cancer, Herceptin, or Roche UK, and it did not have any more information on this other than what had been provided.

Roche noted that the leader of the patient group was invited in a personal capacity to talk to staff at Roche Pharma Development about her experiences of living with breast cancer. Roche noted that what the statement in its response that the lady 'had subsequently set up' the patient group meant was that she was known to the company as a person living with breast cancer and who, after being treated with Herceptin, subsequently set up the patient group not that she had set up the organisation subsequent to her presentation to Roche in December 2005.

Roche submitted that it had no involvement in the development or content of the HER2 testing website. Roche UK did not use this website to 'promote' Herceptin prior to licence. The Roche UK website allowed access to information on products. In the product section, if Herceptin was selected the viewer would only be shown the summary of product characteristics and the patient information leaflet which was in line with Clause 21. In addition a separate section of this website was intended for members of the media and contained archived media releases which could be searched using key words. The media release identified by the complainant concerned the HERA study and had been discussed in detail above. The HER2status website was referred to at the bottom of the release under the heading further information.

Roche had not promoted this website in any promotional materials. The investor relations update referred to by the complainant was from Roche Basel on the corporate site in Switzerland.

Roche did not reject the assumption that there were links between Roche UK and its headquarters in Switzerland however the Code covered activities conducted in the UK itself; Switzerland and other Roche affiliates adhered to their own country codes of conduct. The interest from the media, oncologists, and the public in Herceptin was unprecedented and was due to this being an exceptional treatment heralding a new era of treatment in breast cancer. This opinion was substantiated by statements from oncologists, leading scientific journals and government agencies such as NICE which noted that 'survival of this magnitude due to therapeutic intervention have rarely been recorded in women with metastatic breast cancer'. This was an important statement which reflected the opinion of experts in oncology as well. It was not surprising therefore that this changed the management of metastatic breast cancer but because of the need for HER2 testing and cardiac monitoring it was a complex situation to manage in the NHS.

Roche submitted that the results of the adjuvant trials presented at ASCO resulted in more interest. When these results were finally published in full in the NEJM, October 2005 an editorial included the statements 'The results are simply stunning. With very brief follow-up (one to two and a half years), all three trials show highly significant reductions in the risk of recurrence of a magnitude seldom observed in oncology trials. In fact only tamoxifen administered for five years …in primary breast cancer produces a 50% reduction in the risk of recurrence. Many recent phase 3 trials of adjuvant systemic therapy highlighted absolute benefits of 2 to 6 percent after four to six years of follow up. In contrast, an absolute difference of 6 percent is evident in the HERA trial at two years, with a benefit of 8 percent in the joint analysis …By four years these two trials project an absolute benefit of 18 percent, exceeding all previously reported therapeutic benefits in breast cancer'. The editorial went on to state, 'This observation suggests a dramatic and perhaps permanent perturbation of the natural history of the disease, maybe even a cure'. Moreover it also stated 'On the basis of these results, our care of patients with HER2 positive breast cancer must change today'. The NEJM did not make such statements lightly nor frequently. The immediate and long-term interest generated in the UK by these results had been a challenge for Roche and many other relevant institutions to manage but it firmly believed that it had not exacerbated or encouraged unwarranted expectations. Roche had always tried to work with the regulatory bodies, NICE and the NHS to reach a satisfactory outcome. Roche understood the difficulties that PCTs and commissioners faced but considered that it had acted appropriately and within the Code, as concluded by the Panel and hoped that the additional information outlined above clarified the further points raised.

FURTHER COMMENTS FROM THE COMPLAINANT

The complainant noted that the overarching point of the complaint and appeal was that there was a general background of promotional activity by Roche global and Roche UK that had substantially contributed to untoward actions by senior policy makers. This background activity had been reinforced by the identifiable activities of Roche in the UK that occurred before the grant of the marketing authorization and were promotional in nature. The activity relating to the ASCO conference was a key starting point in this background activity and whilst presumably supported by Roche global helped to promote Herceptin for early breast cancer around the world. The media release by Roche UK, the issue of early HER2 testing, and the HER2 testing website were specific examples of the reinforcement of the results of the earlier and more general promotional activity.

The complainant noted that whilst there might be evidence for the use of HER2 testing in other ways away from direct treatment, Roche's approach did not appear to be about a concern for achieving the best prognostic advice for the patients. If only 38% of patients were being HER2 tested 5 years after Herceptin's licence for metastatic disease why had the company not addressed this issue earlier? Goldhirsch *et al* was a recent paper that had no bearing on the approach that the company appeared to display 18 months ago.

Statements by Government officials were about HER2 testing in anticipation of the use of Herceptin for early breast cancer, not about establishing a prognosis for patients. The statements were seen by many to conflict with pre-existing national policy and possibly undermine the independence of the EMEA licensing process and NICE appraisal. Given that this NHS activity could be seen as promotion before the grant of the marketing authorization for Herceptin it was unwise of Roche to be directly involved in this initiative particularly when it had not sought in the past to support its extensive knowledge of HER2 testing with direct financial support. It appeared that Roche assumed that ministerial support would protect it from any accusation of undue promotional activity at this time. It was not part of Roche's business, at this early stage of seeking a licence, to encourage HER2 testing so that patients who tested positive would expect to have Herceptin and to see its licensing as inevitable.

The complainant alleged that Roche's press release of 13 May 2005 was both part of the general background promotional activity that contributed to pressure from patients and clinicians and also specifically encouraged HER2 testing as a necessary way in to establishing a need for Herceptin. The pressure was such that the perceived need for Herceptin would be established before obtaining marketing authorization and a favourable view of cost effectiveness. As such, the parts of this press release highlighted in relation to HER2 testing were further demonstrations of Roche's approach to stimulating public opinion in support of the wider use of Herceptin.

The complainant alleged that correspondence between Roche and a local cancer network was an example of the action that Roche took to implement its support for HER2 testing. Whilst it was obviously sensible to have a contractual relationship, Roche was promoting the need for Herceptin at an early stage when it should not have been. This correspondence was passed on by a colleague and it reflected their comments and concerns.

The complainant noted that there was a fine line between sponsorship that supported the reasonable dissemination of clinical information and that which contributed towards an opportunity to promote a new treatment so that unbalanced optimism was created at an early stage. Roche did not take sufficient control of ensuring that the dissemination of the information was reasonable and balanced at a stage when Herceptin was not licensed for early breast cancer anywhere in the world. Roche failed to acknowledge the role that it played at events such as the ASCO conference. There was also research to support the view that conference presentations were misleading and over optimistic when compared to the later publication of full trial results in peer-reviewed journals (Dundar *et al* 2006). The media reporting of scientific meetings was also seen as misleading (Schwartz *et al* 2002).

The complainant alleged that 'unplanned' in relation to the ASCO conference presentation was clearly a relative term in this context. The Roche UK media release relating to the research was dated 13 May 2005. The annual ASCO conference was from 14-16 May 2005 with the HERA trial results presented on the last day. As breast cancer was common a number of celebrities had had publicity when they had been diagnosed with the condition. As the ASCO conference was about impressing clinicians the complainant doubted that Kylie Minogue's diagnosis and the related news coverage played much part in promoting Herceptin. The sort of approach that was taken to the annual ASCO conference could be illustrated by a section on the Forbes website. Whilst this web page was about another company preparing for the ASCO conference in May 2006 it illustrated the nature of the conference.

The complainant did not understand the point that Roche was making in relation to the press release dated 13 May 2006. This press release, which was originally submitted in the appeal, appeared to promote Herceptin before it was licensed for early stage breast cancer, anticipated the presentation of the HERA results and was inappropriate in the UK according to the Code. In this sense Herceptin was not then a prescription only medicine as the quote of Clause 20.2 appeared to claim.

The complainant noted that he had asked to see further examples of the press releases that Roche claimed to have issued to counter the misinformation that was common amongst patients and the media. However, Roche's media statement of 6, February 2006 provided no further evidence to substantiate this. As a media statement it did not appear to be an exact copy from an original press release and there were errors in it such as in the incomplete reference. Its primary purpose and content would not suggest that it was about correcting mis-reporting and a prevalent view that Herceptin was a 'cure'. The statement only seemed to repeat the limited information given in other releases and did not present a balanced view of the information then available.

The complainant stated that it was unfortunate that Roche could not provide reassurance about the details of the use of the PR agency as suspicions had been raised in the national media as referenced in The Guardian (29 March 2006) (Case AUTH/1819/4/06). Also, Roche made no mention of the fact that the advertising agency that it had used for Herceptin, and the PR company were both owned by the same group. Presumably Roche either did not know about this link or did not wish to draw attention to a potential conflict of interest.

The complainant alleged that Roche did not adequately address the issue about its press release 13 May 2005 which clearly referenced a website that linked HER2 testing to Herceptin treatment for early breast cancer. Roche seemed to suggest that a media release accessed through the Roche UK website was not promotional because Roche did not see this as promotional material. Websites and press releases such as these were about the promotion of a product or an idea. Given that the promotion was to an unknown public either directly through the internet or indirectly through the media it was impossible to know to what degree the promotion had occurred. Nonetheless the intention was clear.

The complainant considered that an appropriate investor update through a press release might be a part of commercial life but the point of including the Roche global press release of April 2005 was to demonstrate how Roche UK's actions were tied in to their headquarters' actions and accountability could not be avoided.

The complainant alleged that the train of events that led to the widespread interest in Herceptin was initiated by the release of information at ASCO's conference in 2005. Roche must have had some control over this even if it could not predict how far the publicity would go. Roche UK supported this promotion of the early information and did itself little service by quoting the editorial in the NEJM, October 2005. The use of the words, 'simply stunning' and, 'maybe even a cure', supported the view that Roche wished to spread an over optimistic view of a medicine recognised as having some reasonable effects but certainly not seen as being a cure. This was also not helped by the recognition that the editorial's author was a paid consultant of Roche's commercial partner, a fact that it was not necessary to declare in the editorial.

The complainant alleged that he had added some additional information to substantiate the nature of the early promotional activity around Herceptin. The

early publicity at the ASCO conference initiated a complex chain of events. It achieved an unprecedented degree of promotion and caused considerable problems in the UK and for this Roche needed to be accountable.

APPEAL BOARD RULING

The Appeal Board noted that Herceptin had originally been authorized for the treatment of patients with metastatic breast cancer whose tumours overexpressed HER2. It was thus crucial that a patient's HER2 status was known and the Appeal Board noted the submission that establishing this at primary diagnosis was preferable to having to establish it once a patient had developed metastases. The DoH and a national cancer charity had both endorsed such action. Roche's funding of the service would benefit patients and the NHS; there was no evidence before the Appeal Board that the service had been linked to the promotion of Herceptin as alleged. The Appeal Board upheld the Panel's ruling of no breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board considered that any interaction between the patient group or one of its members and Roche was bound to attract attention. Nonetheless the Appeal Board had no evidence to show that the interaction between the breast cancer patient and Roche had compromised the position of either. Neither the patient nor the patient group had received any payment. Whilst the managing director of Roche had met the patient group there was no evidence to show that Herceptin had been discussed or that this meeting was otherwise inappropriate. The Appeal Board upheld the Panel's ruling of no breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board noted that the patient group had received help from a PR agency via an ex employee of Roche who worked for it. Roche in the UK did not employ the PR agency; it appeared that the only link between Roche and the PR agency was through a Roche global team based in Switzerland, which had worked with the agency on one meeting. The Appeal Board found no evidence that Roche had influenced or supported the patient group through the PR agency as alleged and so it upheld the Panel's ruling of no breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board noted the complainant's reference to direct patient contact by Roche as reported in The Guardian; this had been considered in Case AUTH/1819/4/06 wherein no breach of Clauses 20.1 and 20.2 was ruled. In the present case the Appeal Board did not consider that the evidence before it showed, on the balance of probabilities, that Roche had attempted to recruit a patient to promote Herceptin, that it had promoted Herceptin to her or that it had encouraged her such that she would ask her doctor to prescribe Herceptin. The Appeal Board thus upheld the Panel's rulings of no breaches of Clauses 20.1 and 20.2. The appeal on this point was unsuccessful.

The Appeal Board did not consider that the email from Roche to the correspondent at the International Herald Tribune promoted Herceptin. The email was principally about Roche's funding of HER2 testing not about Herceptin. The Appeal Board upheld the Panel's ruling of no breach of Clause 20.1. The appeal on this point was unsuccessful.

The Appeal Board noted that the website HER2status.com was developed and produced by Roche in Switzerland. Roche UK had submitted in its response to the Panel that it had not promoted the site in the UK. The Appeal Board noted from the Roche representative that the website had been aimed at members of the public/patients in the US where promotion of prescription only medicines to the public was permitted.

The Appeal Board noted that a Roche UK press release dated 13 May 2005 had included the HER2status.com web address under further information. The Appeal Board noted from the Roche representative that the press release had been circulated, *inter alia*, to the lay media in the UK. The Appeal Board noted that it had not been provided with a copy of the website contemporary to the 13 May 2005 press release. The relevant Code at that time was the 2003 edition. The HER2status.com website as at 28 April 2006 stated that 'Herceptin Shows Positive Interim results in Early-Stage HER2-Positive Breast Cancer'. The relevant Code at that time was the 2006 edition. The website was currently under revision. The Appeal Board noted that the 13 May 2005 press release remained available on the archive of the Roche UK website.

Taking all the circumstances into account and in particular noting that the website was aimed at members of the public in the US, the Appeal Board inferred that on the balance of probability at the relevant time, the site promoted prescription only medicines to the public. The Appeal Board thus considered that the reference in the press release dated 13 May 2005 and aimed at the lay UK media to a website aimed at a lay US audience, amounted to promotion of a prescription only medicine to the public. The Appeal Board ruled a breach of Clause 20.1 of the Code. The appeal on this point was successful.

The Appeal Board noted its rulings of no breach of the Code above and consequently upheld the Panel's ruling of no breach of Clause 2. The appeal on this point was unsuccessful.

Complaint received	**30 June 2006**
Case completed	**12 January 2007**

CASE AUTH/1888/9/06

VOLUNTARY ADMISSION BY BAYER

Breach of undertaking

Bayer voluntarily advised the Authority that a leaflet which ought to have been withdrawn pursuant to the provision of the undertaking in Case AUTH/1813/3/06 had subsequently been displayed at an exhibition stand at The British Association of Urological Surgeons (BAUS) conference on 29 June.

The Director decided that as the matter related to a breach of undertaking it was sufficiently serious for it to be taken up and dealt with as a complaint under the Code.

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

The Panel noted that the leaflet in question had been dispatched for use at BAUS prior to Bayer being advised of the Panel's ruling in Case AUTH/1813/6/06. Further to the provision of the undertaking on 30 May the leaflet was subsequently displayed in error at BAUS on 29 June. Other material sent to BAUS and caught by the undertaking was not similarly displayed.

The Panel queried whether an email dated 9 June instructing staff about the withdrawal of the material was adequate. It began 'As a result of a complaint from Lilly and following discussions with the ABPI code of practice, Bayer have agreed to remove all reference to …'. It was not clear from the email that Bayer was required to withdraw the material as a result of a ruling of a breach of the Code; by stating that Bayer had agreed to withdraw the material it appeared that such action was a result of informal discussions between it, Lilly and the 'ABPI code of practice'. It was beholden upon companies to ensure that the information they gave to their employees about materials ruled in breach of the Code was clear. Nonetheless the email listed the leaflet as one of thirteen items that were to be withdrawn with immediate effect.

The Panel considered that, despite Bayer's submission that failure to withdraw the leaflet was an oversight, the company had breached its undertaking. A breach of the Code was ruled which was accepted by the company. The Panel further considered that Bayer had not maintained high standards and had brought discredit upon, and reduced confidence in, the pharmaceutical industry. Breaches of the Code were ruled which were upheld upon appeal, including the Panel's ruling of a breach of Clause 2. The Code of Practice Appeal Board also decided to require an audit of Bayer's procedures in relation to the Code.

Upon receipt of the audit report and Bayer's comments upon it the Appeal Board noted that there was much work to be done by Bayer on its standard operating procedures. This was a matter of urgency. Taking all the circumstances into account the Appeal Board decided that Bayer should be reaudited in July 2007.

Bayer plc, Pharmaceutical Division, voluntarily advised the Authority that a leaflet (ref 6LEVI13) which ought to have been withdrawn pursuant to the provision of the undertaking in Case AUTH/1813/3/06, had subsequently been displayed at an exhibition stand at The British Association of Urological Surgeons (BAUS) conference on 29 June 2006.

COMPLAINT

The Director decided that as the matter related to a breach of undertaking it was sufficiently serious for it to be taken up and dealt with as a complaint under the Code. Bayer was asked to respond in relation to Clauses 2, 9.1 and 22 of the Code.

RESPONSE

Bayer explained that the inadvertent use of the leaflet following on from its undertaking to withdraw all materials incorporating the 10 minute claim at issue in Case AUTH/1813/3/06 was a complete oversight. Nevertheless Bayer agreed that such an omission constituted a breach of Clauses 2, 9.1 and 22.

Promotional materials for the stand were despatched to the exhibitor managing the stand at BAUS in early May, prior to the Panel's ruling on the 10 minute claim on 19 May and prior to the company's undertaking to no longer use materials containing the 10 minute claim dated 30 May.

Prior to attending BAUS, Bayer knew that some items it had planned to use could no longer be displayed on the stand eg reprints of Montorsi *et al* (2004) (10 minute study) and a poster containing the 10 minute claim. The staff manning the stand failed to realise that the leaflet at issue also contained the 10 minute claim and therefore should not have been used. In error, it was displayed on the stand. As a result of this error, procedures were now in place to ensure that no materials appeared on a stand without approval of key personnel.

Bayer provided copies of its relevant standard operating procedure (SOP) which it submitted was adequate. The problem in this instance was non-

adherence to the SOP which it was confident would not happen again.

Bayer also provided a copy of an email announcing the withdrawal of, *inter alia*, the leaflet at issue as a result of the ruling in Case AUTH/1813/3/06.

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.

Case AUTH/1813/6/06 concerned Levitra and the SortEDin10 campaign; breaches of the Code were ruled, *inter alia*, in relation to promotion of the efficacy of Levitra 10 minutes after dosing.

The Panel noted that the leaflet in question had been dispatched for use at BAUS prior to Bayer being advised of the Panel's ruling in Case AUTH/1813/6/06. Further to the provision of the undertaking on 30 May the leaflet was subsequently displayed in error at BAUS on 29 June. Other material sent to BAUS and caught by the undertaking was not similarly displayed.

The Panel queried whether the email dated 9 June instructing staff about the withdrawal of the material was adequate. It began 'As a result of a complaint from Lilly and following discussions with the ABPI code of practice, Bayer have agreed to remove all reference to …'. The email did not refer to any rulings of the Panel and so it was not clear that Bayer was required to withdraw the material as a result of a ruling of a breach of the Code; by stating that Bayer had agreed to withdraw the material it appeared that such action was a result of informal discussions between it, Lilly and the 'ABPI code of practice'. It was beholden upon companies to ensure that the information they gave to their employees about materials ruled in breach of the Code was clear. Nonetheless the email listed the leaflet as one of thirteen items that were to be withdrawn with immediate effect.

The Panel considered that, despite Bayer's submission that failure to withdraw the leaflet was an oversight, the company was in breach of its undertaking and had not maintained high standards. Breaches of Clauses 22 and 9.1 were ruled. The failure to withdraw the leaflet had brought discredit upon, and reduced confidence in, the pharmaceutical industry; a breach of Clause 2 was ruled.

APPEAL BY BAYER

Bayer submitted that the Panel's decision to treat this as a serious breach and so invoke Clause 2 of the Code was unreasonable. The consequences of the ruling, especially the requirement to publish Bayer as having 'brought discredit upon and reduced confidence in the pharmaceutical industry' were disproportionate. The 'discovery' by a Lilly employee that one of sixteen withdrawn promotional pieces was inadvertently displayed at one meeting was not comparable to serious breaches of the Code, especially recent examples of breaches of Clause 2. Nor did the company consider that it should be regarded as having failed to maintain high standards (Clause 9.1) for a single omission of a minor nature.

Bayer submitted that following receipt of the Panel's ruling in Case AUTH/1813/3/06, it was made very clear to employees that all materials in which the claim in question was used had to be withdrawn immediately. The instruction was in accordance with Bayer's SOP. On reviewing another SOP about the withdrawal of promotional materials no longer compliant with the Code, Bayer had decided to add that the '[Marketing Manager] will be responsible for checking additional distribution routes for the materials in question and preventing any usage'. This would deal with the situation arising in this case.

Bayer submitted that in this case, sixteen such items were identified, including the leaflet at issue. In one instance, this single piece was inadvertently displayed at a congress. All of the materials for this congress had been ordered for distribution prior to the Panel ruling but during the process of intercepting these materials, the company which was building the exhibition stand on Bayer's behalf overlooked the leaflet in question. This was subsequently identified by an employee of Lilly who approached Bayer about this oversight. In discussion with Lilly, Bayer agreed to voluntarily admit a breach of the Code to the Authority. Bayer had accepted that the undertaking given not to utilise these pieces further had been breached and also that this was not a trivial issue.

Bayer submitted that the Panel's ruling of breaches of Clauses 2 and 9.1 was out of proportion, especially with the decision to name and shame the company as bringing discredit upon the industry by this regrettable administrative oversight. If the Appeal Board upheld a breach of Clause 2, then it asked that consideration be given not to require such a breach to be publicised in the medical and pharmaceutical press on the basis that published breaches of Clause 2 were usually related to deliberate flouting of the Code.

Bayer referred to a number of past cases which concerned breaches of Clauses 2 and 9.1 of the Code.

APPEAL BOARD RULING

The Appeal Board noted from Bayer's representatives that the leaflet in question together with a number of other items had been dispatched for use at BAUS prior to Bayer being advised of the Panel's ruling in Case AUTH/1813/6/06. The agency responsible for setting up the stand at the BAUS meeting on 29 June was subsequently supplied with a list of items which were not to be used at the meeting. The leaflet at issue was missing from that list. A Bayer employee was responsible for ensuring that no materials in breach of

the undertaking were displayed on the stand. However, approximately 50 copies of the leaflet at issue were placed on the stand of which approximately 10 were taken. Bayer could not provide exact figures.

The Appeal Board was concerned that material had not been withdrawn as a result of the undertaking. No date for final withdrawal of material had been given in the email from Bayer instructing staff about the withdrawal of material. Bayer's representatives submitted that it relied upon its field force and regional managers to return items. The Appeal Board considered this process inadequate.

The Appeal Board noted from the Bayer representatives that Lilly had written to Bayer on 19 July to advise it that the leaflet at issue had been found on the exhibition stand; the voluntary admission was dated over six weeks later on 1 September. The letter from Lilly had not been provided by Bayer. Bayer's representatives submitted that the delay in sending the company's voluntary admission to the Authority was due to intercompany communications concerning this and other matters. The Appeal Board considered this explanation to be inadequate.

The Appeal Board considered that Bayer's email of 9 June instructing staff to withdraw material was inadequate. It began 'As a result of a complaint from Lilly and following discussions with the ABPI code of practice, Bayer have agreed to remove all reference to …'. The email did not refer to any rulings of the Panel and so it was not clear that Bayer was required to withdraw the material as a result of a ruling of a breach of the Code; by stating that Bayer had agreed to withdraw the material it appeared that such action was a result of informal discussions between it, Lilly and the 'ABPI code of practice'. It was beholden upon companies to ensure that the information they gave to their employees about materials ruled in breach of the Code was clear. The Appeal Board considered that the email sought to downplay the situation. Nonetheless the email listed the leaflet as one of thirteen items that were to be withdrawn with immediate effect.

The Appeal Board 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 and of self-regulation that companies complied with undertakings.

The Appeal Board noted that Bayer had accepted the Panel's ruling of a breach of Clause 22. In failing to withdraw the leaflet, the company had not maintained high standards. The Appeal Board upheld the Panel's ruling of a breach of Clause 9.1. The failure to withdraw the leaflet had brought discredit upon, and reduced confidence in, the pharmaceutical industry. The Appeal Board upheld the Panel's ruling of a breach of Clause 2. The appeal was unsuccessful.

The Appeal Board was concerned that Bayer's original voluntary admission was not a full and fair account of all the circumstances, and further it was concerned about the apparent failings in Bayer's procedures to comply with undertakings given in respect of the Panel's rulings. The Appeal Board was also concerned that the email of 9 June was inadequate. The Appeal Board decided in accordance with Paragraph 10.4 of the Constitution and Procedure to require an audit of Bayer's procedures in relation to the Code.

CONSIDERATION OF THE AUDIT REPORT BY THE APPEAL BOARD

Upon receipt of the audit report and Bayer's comments upon it the Appeal Board noted that there was much work to be done by Bayer to produce, implement and train out standard operating procedures. This was a matter of urgency. Taking all the circumstances into account the Appeal Board decided that Bayer should be reaudited in July 2007.

Proceedings commenced	**4 September 2006**
Undertaking received	**18 December 2006**
Appeal Board consideration	**22 February 2007**

CASE AUTH/1895/10/06

ANONYMOUS v ASTRAZENECA

Inappropriate hospitality

An anonymous complainant complained, *inter alia*, about AstraZeneca's provision of hospitality to members of various national associations for asian psychiatrists working in the UK. The complainant drew particular attention to meetings held in Pakistan in 2004, Coventry in 2004, India in 2005 and Sri Lanka in 2005, sponsored by AstraZeneca and organised by the South Asian Forum (SAF).

The complainant alleged that these meetings were more of a get together and based on similar cultures/religions rather than recognized academic meetings.

The Panel noted the complaint was about the whole situation as well as the individual meetings. It appeared that SAF organised annual meetings and AstraZeneca was a major sponsor. Eleven doctors had been sponsored by AstraZeneca to each attend the meetings; Colombo (July 2005), New Delhi (February 2005) and Lahore (September 2004) in the space of ten months. The Panel was generally concerned about the arrangements and impression given. It considered each event separately.

The Panel noted that there was no agenda and no details of delegates or costs for the meeting in Coventry. The only item provided was an invitation letter which referred to the first West Midlands, South Asian Forum meeting, which was created by SAF. It appeared that the business of the forum was dealt with on the Friday evening and the clinical and scientific programme was held on the Saturday morning. This was at odds with one of the presentation slides which stated that the business meeting ran from 9.30am to 10am on the Saturday morning. The clinical lectures ran from 10am until 12.45pm. A corporate presentation on AstraZeneca was given on the Friday evening.

The Panel was concerned that no details were available about the costs, or the list of delegates or the final programme. The Panel did not consider a meeting of just 4.5 hours in total justified overnight accommodation.

The Panel noted that only a small number of delegates stayed on the Friday evening. The reason given by AstraZeneca was due to significant travel. The Panel queried this given the regional nature of the meeting. The Friday evening was not part of the meeting as such as most of the delegates had not attended. On balance, the Panel did not consider that the overnight stay was justified and thus a breach of the Code was ruled. The Panel did not consider that the circumstances warranted any rulings of further breaches of the Code including Clause 2.

The Panel considered that from the programme for the meeting in Lahore the scientific/educational content was not unreasonable for sponsorship by a pharmaceutical company or for delegates to be sponsored to attend. The sessions ran generally from 9am – 5pm on each day. The programme stated that AstraZeneca was the sole sponsor for UK delegates via an unrestricted grant which covered economy air fare, five nights' stay at a hotel, subsistence and World Psychiatry Association (WPA) registration.

The Panel noted from AstraZeneca's submission that a live folk music presentation had been arranged by the SAF. AstraZeneca stated that it had no part in the invitation, arrangement, promotion or logistical facilitation of this event.

The memorandum of understanding between AstraZeneca and SAF stated that the total cost per invited person was approximately £1100. The total educational grant from AstraZeneca was £55,000. All costs should be within this budget including AV costs, speakers (2 or 3) and any additional meeting costs. This would fund 50 to 55 delegates. The invitation to delegates referred to the need to comply with the Code.

The Panel was, however, concerned to note that the memorandum stated that AstraZeneca representatives were to invite UK delegates from early 2004 'to reap benefit from beginning of year'.

Nonetheless, taking all the circumstances into account the Panel considered that the sponsorship by AstraZeneca for the meeting was not unacceptable and no breach was ruled.

The Panel considered that from the programme for the meeting in New Delhi the scientific/educational content was not unreasonable for sponsorship by a pharmaceutical company or for delegates to be sponsored to attend. There were two half day sessions and two full day sessions plus an AstraZeneca satellite symposium for UK delegates. The educational grant (around £114,000) was to cover travel, 3 nights' accommodation, subsistence and registration fee for 70 delegates.

The Panel noted that attendance at the conference necessitated a three night stay but 23 of the delegates sponsored by AstraZeneca (29%) travelled out earlier or returned later than the AstraZeneca appointed times with an average length of stay of 14 days. AstraZeneca submitted that the additional costs incurred by such changes were to be paid by delegates.

The Panel was concerned that delegates, including

AstraZeneca staff, had taken the last day out of the conference to visit the Taj Mahal. This was not arranged or facilitated by AstraZeneca nor was it part of the programme but nevertheless the Panel considered that the participation of AstraZeneca staff on such an outing which meant missing some of the sessions gave a poor impression.

Taking all the circumstances into account the Panel considered that the sponsorship by AstraZeneca for the meeting was not unacceptable and no breach of the Code was ruled.

The Panel considered that from the programme for the meeting in Colombo the scientific/educational content was not unreasonable for sponsorship by a pharmaceutical company or the delegates to be sponsored to attend. There was one half day session and four full day sessions plus an AstraZeneca satellite symposium for UK delegates.

AstraZeneca funded travel and accommodation for 105 delegates covering flights, 5 nights' accommodation, subsistence and WPA registration fee.

The Panel was again concerned that a number of delegates travelled outside the AstraZeneca appointed times but it was made clear that all additional costs were to be paid by delegates.

Taking all the circumstances into account the Panel considered that the sponsorship by AstraZeneca for the meeting was not unacceptable and no breach of the Code was ruled.

The Panel noted that AstraZeneca had sponsored the entire costs of the meeting in Birmingham for 57 delegates. The educational part ran for 1.5 hours on the Friday evening and from 9.30am until 3.30pm on the Saturday (including refreshment breaks). From the programme the Panel considered that the scientific/educational content (6.25 hours) was not unreasonable for sponsorship by a pharmaceutical company or for delegates to be sponsored to attend. Taking all the circumstances into account the Panel considered that the sponsorship by AstraZeneca for the meeting was not unacceptable and no breach was ruled.

The Panel considered that from the programme for a meeting in Dubai the scientific/educational content was not unreasonable for sponsorship by a pharmaceutical company or for delegates to be sponsored to attend. There were two half days and three full day sessions.

AstraZeneca was to sponsor 80 UK delegates. It would pay flight costs, accommodation, subsistence and WPA registration fee ie approximately £1,670 per delegate.

The Panel was concerned that two musical presentations were included albeit that these were arranged independently of AstraZeneca by SAF and the hotel. In the Panel's view the musical presentations did not mean that the two dinners were wholly or mainly of a social nature.

The Panel considered that the subsistence offered appeared to be appropriate and not out of proportion to the occasion. It considered that the costs (around £1,670) were high and queried whether they were in line with the level that recipients would normally adopt when paying for themselves.

However, taking all the circumstances into account the Panel considered that the sponsorship by AstraZeneca for the meeting was not unacceptable and no breach of the Code was ruled.

An anonymous complainant complained about the activities of a number of companies, including AstraZeneca UK Limited.

COMPLAINT

The complainant stated that in the last few years, a few psychiatrists had established a very close personal relationship with pharmaceutical companies. These psychiatrists had been using pharmaceutical companies for their personal advantages, benefits, ambitions and personal growth. They had established the South Asian Forum (SAF), which organised meetings for its members in the UK as well as places such as in India, Pakistan and Sri Lanka. All the expenses of hotel, travel and food were 'sponged' by pharmaceutical companies. Until recently AstraZeneca had 'sponged' Asian psychiatrists to travel to Pakistan in 2004, to India in January 2005, to Sri Lanka in July 2005. All these psychiatrists were friendly to each other and enjoyed these meetings as an opportunity to meet each other. They invited them to attend the meetings and money was paid by pharmaceutical companies. They maintained the database of most of the Asian and Arabic psychiatrists. It was a numbers game. They had numbers to influence the pharmaceutical companies and pharmaceutical companies tried to oblige the vulnerable psychiatrist who could increase prescriptions.

Surprisingly a meeting in Lahore (Pakistan) in 2004 was organised by a UK psychiatrist and his cousin in Pakistan. It was believed that about 100 health professionals were taken to Pakistan at the expense of AstraZeneca. The psychiatrists who went to Pakistan enjoyed a holiday and a large number were able to meet their family. It was worth investigating the list of delegates at that meeting, who invited them, how the money was paid. It was worth investigating as to whether the money was paid directly to the organisers and they organised a flight, hotel and other expenses. There were rumours that £1,400 per psychiatrist was paid by AstraZeneca to the organisers, to include all the expenses. The organisers (a few psychiatrists) had a meeting at a Coventry hotel in the UK to organise this meeting.

It was very important to investigate the list of participants who went to India, Sri Lanka and Pakistan. It was also important to check with the

participants who invited them, who motivated them and how money was paid for their visits. Interestingly it was decided who would go or not go to the outside UK meeting by two or three psychiatrists most of the time. These few psychiatrists invited delegates by email, telephone and post. They might be able to provide the addresses of the psychiatrists to pharmaceutical companies. In this kind of meeting they organised a fascinating Asian cultural programme that was also a motivating factor to attend.

It would be worthwhile to note that these kinds of meetings were more of a get together and based on similar cultures/religions not internally recognized academic meetings. The majority of delegates were attending again and again. There was a numbers game, this group could manage more than 100 psychiatrists to attend the meeting and it influenced the pharmaceutical companies to breach the Code. This numbers game and desire of a few psychiatrists for using pharmaceutical monies for their personal advantage/growth tempted pharmaceutical companies.

It was also worth investigating that two psychiatrists arranged a meeting of their common friends in Coventry, in 2004; all the participants were able to have free hotel and food. This gave a good opportunity to meet friends and have a weekend break. If funding was not available from pharmaceutical companies, not a single person would go to attend a South Asia Forum meeting outside the UK or within the UK. It was worth investigating the hotel in Coventry where two or three psychiatrists have had many personal meetings of friends/organizers and all the expenses were paid by AstraZeneca.

This South Asian Forum was a regional association and should not grow on the basis of pharmaceutical money. This association also closely worked with the Islam Association; about fifty percent of delegates were in common. One of the above psychiatrists had been instrumental in these two associations. These two associations would disappear within a few weeks if not days if they did not have financial support from pharmaceutical companies. It was evident that initially for two to three years one named company supported these kinds of meetings.

Motivating factors for participants:
1 Free hotel and sense of holiday; find it a nice weekend break.
2 Meeting common friends.
3 Enjoying night cultural programme.
4 In the night enjoying Asian food.

Motivating factors for organizer:
1 They tried to influence and build up relationships with world prominent psychiatrists who they invited as speakers and then used them for personal growth.
2 They reflected their strength to those who were contesting for any post in World Psychiatrist Association (WPA) and got closer to them.

Motivating factors for pharmaceutical companies:
1 Take advantage of numbers and try to push their sales.
2 Need for investigation to establish whether there has been a breach of the Code.
3 Was it appropriate to use pharmaceutical companies for their personal picnic or personal association or personal cultural meetings?
4 Was it appropriate to use pharmaceutical companies for their personal growth and uniting all Asians together and reflecting the numbers and influencing the pharmaceutical companies?
5 It was a two way process, pharmaceutical companies needed the numbers and this group of doctors needed money for their personal agendas.

The complainant asked why AstraZeneca repeatedly 'sponged' meetings such as the South Asian Forum, the Islam Association and meeting in Lahore, India and Sri Lanka.

Why did AstraZeneca sponsor so many psychiatrists to go to Pakistan which was more a holiday rather then an internationally recognized academic conference such as 'eruption' psychiatric conference or world psychiatric association.

Why AstraZeneca again and again sponsored more or less the same people to visit India and then Sri Lanka and Pakistan.

Why were the delegates selected by one or two psychiatrists who had a key role in the South Asia Forum.

Who maintained the database of the psychiatrists and sent the invitations.

Sent with the complaint was the notification and booking form for the South Asian Forum Regional Meeting held in Birmingham on 7 - 8 July 2006. This stated that the meeting was sponsored by AstraZeneca UK Ltd.

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

RESPONSE

AstraZeneca submitted it had not sponsored activities of the Islam Association referred to by the complainant.

It should be noted that during the period between early 2004 to the current time, the environment had evolved and some of the standards that applied to meetings arrangements had changed. AstraZeneca policies and procedures had also adapted in step and a rigorous external meetings policy was put in place in 2005. Therefore AstraZeneca requested that the historical context for these meetings was borne in mind when reviewing the arrangements made for them, specifically for those meetings up to and including the Colombo meeting in mid-2005.

1 The South Asian Forum (SAF) and the British Indian Psychiatrists Association (BIPA) AstraZeneca's partnership

1.1 History of SAF

SAF was formally known as the South Asian Forum on Mental Health & Psychiatry; it was an international group set up with multiple aims that comprised mainly of academic work, charitable acts, advising governments and international networking. These aims and objectives were consistent with other British South Asian doctors groups eg British Association of Indian Anaesthetists, British Association of Physicians of Indian Origin, the Association of Pakistani Physicians and Surgeons of the United Kingdom. One of the principal aims of SAF was to provide a forum for the members to establish academic and professional links with other associations or groups that were working in the field of mental health. SAF had offices/chapters in several countries worldwide to administer SAF aims and objectives locally. SAF chapters might combine efforts in order to meet SAF international aims and objectives. The UK chapter of SAF would be referred to as SAF UK. There was no official membership however, the SAF events were open to all with an interest in the SAF aims and objectives. SAF UK maintained its own database of Asian psychiatrists in the UK.

In 1997, three psychiatrists formed a working group to create and formalise SAF (without any AstraZeneca involvement). This group then worked through to the formal launch at an international meeting held in Colombo in April 2002 – again without any AstraZeneca involvement. SAF was an independent group and was not wholly reliant on the pharmaceutical industry for support. AstraZeneca supported certain educational activities in partnership with SAF. SAF organised other activities that were run independently of AstraZeneca sponsorship but were funded by donations and relief work (www.southasianforumpsychiatry.com). SAF UK aimed to contribute to development of mental health services in other SAF chapter countries. To that end SAF chapters collaborated with various professional bodies in different countries to organise international and regional educational programmes. The international programmes were endorsed by the WPA.

AstraZeneca had sponsored some of SAF UK's educational activities because they enhanced the care of South Asian patients both in the NHS and in other countries. SAF reached out to represent approximately 20% of the consultant psychiatrist workforce in the UK. Medical schools in the UK had not historically given a special educational focus to the mental health needs of South Asian patients and this topic represented a significant unmet medical educational need.

AstraZeneca believed that SAF was a legitimate and worthy organisation for the industry to work with. In order to strengthen this professional relationship, AstraZeneca had, over the last 2 years, given considerable guidance to SAF regarding the Code, AstraZeneca Meetings Policy and the high standards that AstraZeneca expected at its sponsored meetings. SAF had been receptive to this guidance and implemented it. An email was provided that set out a three year activities agreement with SAF starting in 2005.

Contrary to the complainant's assertion, AstraZeneca also sponsored delegates attending European psychiatry congresses such as those of the ECNP (European Congress on NeuroPsychopharmacology) and other global congresses such as the APA (American Psychiatric Association).

1.2 History of BIPA

BIPA was set up in 1993 with the aim of providing a forum for practising British psychiatrists of Indian origin. The organisation, which now had over 500 members, provided a forum for psychiatrists, across all grades, to promote, share and encourage research and education in psychiatry in the UK for the improvement of mental health services for people of Indian origin.

BIPA was an independent organisation and did not rely solely on funding from the pharmaceutical industry. BIPA members paid £40 for annual membership and £175 for life membership (www.bipa.org.uk).

2 Educational meeting in Coventry, 12-13 March 2004

This meeting was organised by the local AstraZeneca sales teams in collaboration with SAF UK. The meeting took place over a Friday evening and Saturday morning in March 2004 with a primary educational purpose. No other pharmaceutical company was involved.

The invitation that SAF used was provided. Since this was a locally organised meeting and took place two and a half years ago, detailed records including a delegate list, costs and a printed agenda were not available. It was believed 30-35 delegates attended the meeting on the Saturday whilst a smaller number that had significant travel to undertake arrived the night before. No delegates stayed on the Saturday night. At least one sales representative attended. AstraZeneca had details of the programme on Saturday morning but not Friday evening. It was believed that delegates received 1.5 hours education on Friday evening including a corporate presentation on AstraZeneca delivered by an AstraZeneca manager, followed by dinner. No entertainment of any kind took place at this meeting. The presentations were provided.

Delegates received 3 hours' education on Saturday morning (9.30-12.45pm including a 15 minute break) on 'Second generation antipsychotics and glucose metabolism', 'Treatment of bipolar disorder – a critical review,' 'Gender and schizophrenia – treatment implications' preceded by a 30 minute SAF business meeting where an overview of SAF was presented to delegates, therefore providing 4.5 hours education in total.

Delegates were invited by both AstraZeneca sales

representatives and via SAF nominations from all over the central region of the UK that contained approximately a third of the UK population. Coventry was a central location and provided conference facilities to meet the needs of a meeting this size. An overnight stay was arranged due to the significant travel that AstraZeneca believed many of the delegates would have needed to undertake.

The venue was not a luxurious or sporting venue and would therefore have been perceived as being secondary to the educational purpose of the meeting. It had recently been renovated and so its accommodation was now significantly superior to that which it provided at the time. No entertainment was provided at this meeting.

AstraZeneca accepted that the retained records for this meeting were incomplete. However, the arrangements were focused on the educational content.

Since 2004 AstraZeneca had fundamentally revised its internal policies and practices, in particular for sales and marketing practices and external meetings. In 2005, an electronic customer relationship management tool was introduced that facilitated record keeping in line with AstraZeneca's new policies and the requirements of the Code. All meetings, be they local or centrally organised, were subject to a rigorous process and had to be validated before invitations were distributed. The meeting agenda and delegate list for all meetings were automatically recorded. In addition, all staff were tested annually on and agreed to fully comply with, the internal policies and the Code. All employees were required to sign understanding and acceptance of their responsibilities. Under the External Meetings Policy, it was understood that a meeting that required significant travel and had at least 6 hours of educational content could warrant an overnight stay.

AstraZeneca did not therefore consider breaches of Clauses 2, 9.1 and 19.1 of the Code to have occurred.

3 WPA regional and inter zonal meeting in collaboration with Pakistan Psychiatric Society, South East Asian Division, South East Asian Division of the Royal College of Psychiatrists, South Asian Forum on Mental Health and Psychiatry, World Association for Psychosocial Rehabilitation, Mental Health Resource Centre (a Pakistani based organisation) in Lahore, Pakistan, "Improving Mental Health in Developing Countries" - 16 - 20 September 2004, Lahore, Pakistan

This was a recognised, independent international congress attended by over 450 delegates and speakers from all over the world. It was endorsed and academically co-sponsored by the internationally recognised WPA.

The meeting and its agenda were organised by SAF UK in collaboration with the aforementioned bodies and independently of AstraZeneca. AstraZeneca was official sole sponsor of this meeting through an unrestricted educational grant of £75,550 paid to SAF UK. Other companies were not precluded from sponsoring delegates to attend. According to the SAF UK one company sponsored 5 delegates, another sponsored 8 delegates and another sponsored 20 delegates. AstraZeneca understood that the funding of the educational activities of academic groups was not unacceptable provided that the company had confidence in that group to make arrangements that were appropriate under the Code.

AstraZeneca's grant was unrestricted with regard to educational content. A Memorandum of Understanding (copy provided) set out terms and conditions for a professional business relationship between AstraZeneca and SAF for the period of this meeting. Since AstraZeneca was attending the meeting, this was a diligent measure to define the working relationship.

AstraZeneca had asked SAF for full meeting details. SAF was the third party recipient of an educational grant and was responsible for making the meeting arrangements including record keeping. AstraZeneca supplied details where able.

SAF was responsible for the meetings arrangements including flights. The unrestricted educational grant covered the cost of economy class return travel to the UK; five nights' stay at a hotel in Lahore, transfers at Lahore and subsistence (including non-alcoholic beverages) and WPA registration. SAF meeting registration (£100) and travel in the UK were not covered by the grant and would have been met by UK delegates.

Lahore was logistically a reasonable location for international speakers and delegates to travel to. Two of the main organisers, Pakistan Psychiatric Society and Mental Health Resource Centre, were based in Pakistan. On this basis, AstraZeneca considered the location justified and appropriate according to the 2003 Code.

3.1 Agenda

A full educational agenda for this meeting endorsed by WPA was provided. It was created independently of AstraZeneca. The five day meeting had 31 hours' educational content (generally from 9am-5pm) in the form of scientific and educational presentations provided by a large number of independent speakers and one poster presentation session. The speakers represented a truly international mix as follows. The UK provided 45 presentations; Pakistan – 50; India - 21; Sri Lanka – 5; Bangladesh – 6; Thailand – 2; USA – 8; Australia – 5; Italy – 7; Malaysia – 2; Switzerland – 2; Kuwait – 2; Canada, New Zealand, Egypt, Greece, Argentina, Sweden, Japan, Finland, Hungary, Malaysia, Bhutan, Brunei provided one each.

SAF arranged a brief live folk music presentation after dinner on one of the conference nights. This acted as a welcome reflecting the local culture and was not uncommon at international congresses. AstraZeneca had no part in the initiation, arrangement, promotion

or logistical facilitation of this event. AstraZeneca did not have prior knowledge of or provide budget funding for nor did it approve this event.

3.2 Delegates and flight details

As the meeting was supported by an unrestricted educational grant, AstraZeneca did not have full records of flight details and so did not know how many delegates had travelled before or after the meeting dates. About £575 per delegate was set-aside for economy class travel from the UK to Lahore. It was intended that the AstraZeneca group (AstraZeneca personnel and delegates) fly out on 15 September (to enable delegates to cope with jet lag and recover after the long flight) and return on 21 September. Delegates changing flights from the group dates would have been responsible for covering additional costs not AstraZeneca.

AstraZeneca invited 77 delegates and 75 attended out of a total of 209 international delegates. The largest international delegation being 94 from India. In addition there were approximately 250 local delegates from Pakistan making a total of over 450 delegates. Therefore, the majority of delegates at this meeting were from outside the UK. The invitation to UK delegates was provided.

AstraZeneca personnel attended, five of whom were sales staff who manned an AstraZeneca promotional stand at the conference. No other company displayed a stand.

3.3 Accommodation and hospitality costs

The unrestricted educational grant covered costs for UK sponsored delegates for the duration of the conference (15 - 21 September). Total budgeted cost per head within the grant was approximately £1,100. This included flight costs, accommodation (£60-80) transfers, WPA registration and all lunches and dinners. Accommodation was arranged at the hotel where most of the educational sessions took place. Delegates who arrived before 15 September or stayed after 21 September had to make their own accommodation arrangements at their own expense. Dinner was provided on the following nights: 'Inaugural Dinner' 8pm, 17 September, 'Concluding dinner' 8pm, 19 September, and 'Dinner by invitation' 8pm, 20 September. AstraZeneca did not have any further information about the dinners.

Summary

AstraZeneca submitted that this educational meeting was arranged by the SAF UK in collaboration with other international and two national (Pakistani) professional associations. The majority of delegates and speakers originated from outside the UK. Economy class flights were arranged in line with conference dates and accommodation was chosen based on its proximity to the conference venues.

AstraZeneca therefore did not consider that it had breached Clauses 2, 9.1 or 19.1 of the Code.

4 International conference on mental health with a symposium on transcultural psychiatry in collaboration with BIPA and the Institute of Human Behaviour and Allied Sciences (IHBAS). (Run as part of the Transcultural Psychiatry Section Meeting of WPA): 'Innovations in Mental Health Services and Research' - 3 - 6 February 2005, New Delhi, India.

AstraZeneca noted that the SAF was not involved in this meeting.

This was an independent international congress attended by approximately 300 delegates and speakers from all over the world. It was endorsed and academically co-sponsored by the WPA. The meeting formed part of the Transcultural Psychiatry Section Meeting of the WPA and was therefore a recognised international congress.

AstraZeneca was the sole officially recognised sponsor of the meeting. Other companies were not excluded from sponsoring delegates to attend.

4.1 Agenda

The invitation sent to UK delegates included the agenda which was created by BIPA in collaboration with IHBAS independently of AstraZeneca.

The meeting was held over 2 full days and 2 half days with a total of 21 hours' scientific and educational presentations provided by a large number of independent international speakers. 15 speakers were from India, 9 from the UK, 2 from Australia and 1 each from Sri Lanka, Egypt, Switzerland and Finland. New Delhi was logistically a good location for all 30 speakers to travel to and one of the main organisers, IHBAS, was based in New Delhi. AstraZeneca considered the location justified and appropriate according to the 2003 Code.

Of the UK delegates invited by AstraZeneca 70 accepted. A condition for being invited was to be a life member of BIPA ie a UK psychiatrist with an Indian qualification or strong interest in Indian psychiatry. AstraZeneca also arranged for 8 UK speakers to attend the meeting. The total number of delegates that attended the meeting was approximately 300.

No entertainment or social activities of any kind were funded or arranged by BIPA. AstraZeneca understood that IHBAS arranged an evening reception for delegates on one of the conference nights but details of this event were not available. No entertainment or social activities were funded or arranged by AstraZeneca as part of the sponsorship arrangements.

On Sunday 6 February, approximately 10 -15 delegates independently, and at their own expense, organised a whole day trip to the Taj Mahal. This day of the meeting had a half-day agenda and there were no formal speaker presentations although there was the option of attending one of three workshops on specialised topics lasting 2 hours. Four AstraZeneca personnel also attended this trip, again at their own

expense. AstraZeneca did not initiate, pay for, promote or facilitate the logistics of any aspect of this trip.

4.2 Delegates and flight details

Most delegates flew out on 2 February 2005 and returned to the UK on 8 February. At that time the flight arrangements would have been consistent with AstraZeneca policy ie group flights were funded and any changes would have been met at the delegate's own expense. Flights were not booked directly by AstraZeneca. Instead, delegates booked their economy class flights themselves through the AstraZeneca appointed travel agent. The agent was then re-imbursed. A briefing to the travel agent from AstraZeneca was provided, setting out guidance for the bookings stipulating that delegates must be in Delhi on the conference dates and that only AstraZeneca delegates should be allowed a booking. Delegates were told in a letter (provided) that accommodation would only be booked on the conference dates so that if flights were booked outside of this period, they would have to bear the accommodation costs for the extra period. AstraZeneca clearly stated that its policy did not allow for spouses or partners, who were not delegates in their own right, to participate in congress-associated hospitality.

Twenty three out of 78 delegates and speakers either flew out a few days earlier or returned a few days later than the AstraZeneca team with an average length of stay of 14 days.

AstraZeneca only provided accommodation for 3 nights during the conference ie 3, 4 and 5 February. Those delegates who arrived before 3 February or left after 5 February had to make their own arrangements.

Sixteen delegates and speakers made their own travel arrangements.

All flights were economy class and cost on average £672 per head.

Nine AstraZeneca staff attended, of whom five were sales staff who manned a promotional stand. No other company displayed a stand.

4.3 AstraZeneca closed satellite symposium

A copy of the invitation to the above symposium entitled 'The Good, the Bad and the Ugly – An update on current thinking in the use of antipsychotics' was provided. This invitation was only sent to UK delegates along with the main invitation and clearly stated the intended audience.

The symposium ran from 5.30pm -7.30pm on 5 February after one of the full conference days at one of the same venues. The symposium comprised of 3 presentations given by independent UK psychiatrists. AstraZeneca reviewed all presentations beforehand to ensure the content was accurate, balanced and in line with internal compliance procedures. The presentations (provided) represented an educational overview of a subject that was in line with the main conference theme. The symposium was followed by dinner at one of the conference venues.

4.4 Accommodation and hospitality costs

Two different hotels were used by AstraZeneca for UK delegates and speakers. Approximately half stayed at one hotel (at a cost of £130 per night) where the conference was held with the other half staying at a second hotel (at cost of £99.50 per night). The hotels were close to each other and the airport. The first hotel was chosen on the basis of its business facilities, which a large conference would demand.

Dinner was provided at the first hotel on the evening of 3 and 4 February with a budgeted average cost per head of £15.58 for food and beverages. On the evening of 5 February delegates were provided dinner at the other conference venue, where a budget for a maximum cost of £40 per head was set aside. AstraZeneca did not have the figure for the final cost. All lunches were served at the first hotel in between sessions, at a budgeted cost of £8.92 per head for food and beverages. The logged costs per head for accommodation and subsistence meals (lunch and dinner) amounted to £179 per head per night.

AstraZeneca also met the delegates' joint WPA/BIPA registration fee for the meeting of £100 per head.

A record of actual spend was provided.

Summary

AstraZeneca submitted that the arrangements and hospitality provided to UK delegates attending the meeting in New Delhi 2005, were in keeping with the main purpose of the meeting, justified and appropriate as required by the 2003 Code.

AstraZeneca therefore did not consider breaches of Clauses 2, 9.1 and 19.1 of the Code had occurred.

5 International Conference on Psychiatry. Organised by the SAF in collaboration with South Asian Division, Royal College of Psychiatrists, UK, Sri Lankan College of Psychiatrists and the World Association for Psychosocial Rehabilitation. Co-sponsored by the WPA. 'Improving access and delivery to mental health care in south Asia' - 24 – 28 July 2005, Colombo, Sri Lanka

This was a recognised, independent international congress attended by 325 delegates and speakers from all over the world. It was endorsed and academically co-sponsored by the WPA.

SAF UK organised this meeting in collaboration with the aforementioned groups. AstraZeneca sponsored UK delegates to attend but was not the sole official sponsor of the meeting. AstraZeneca understood from SAF UK that two other pharmaceutical companies both sponsored 12 delegates each and another sponsored ten. A copy of the invitation sent to UK delegates invited by AstraZeneca was provided.

AstraZeneca met WPA delegate registration fees of £136 per head and delegates met their own SAF registration fees of £150 for this meeting.

5.1 Agenda

The educational agenda, organised independently of AstraZeneca was endorsed by the WPA. The meeting took place over four and a half days with 29.75 hours' educational content that generally took place from 9am-6pm. AstraZeneca held a closed satellite symposium for UK delegates on 25 July from 7pm-8.30pm followed by dinner.

In total, there were 105 opportunities for speakers to present at, or chair a session. These were allocated as follows: UK speakers, 30; Sri Lanka and India, 13 each; Australia and the USA, 11 each; Pakistan, 9, Malaysia, 5, Philippines, 4, Thailand, 3; Bangladesh, 2 and Indonesia, Cambodia, Japan and Italy, 1 each. Therefore most of the speakers/expertise resided around Sri Lanka and from outside the UK. Colombo provided a convenient logistical location for all speakers and delegates to convene, in keeping with the theme of this meeting.

This meeting was designed by SAF to improve access and delivery to mental health care in South Asia and was well attended by delegates from South Asia where mental health services were developing and delegates and speakers from countries where mental health services were better developed. Delegates would have been able to learn from those countries where mental health services were developed and from those countries that were developing, including experience on psychological issues associated with the recent natural disasters affecting people of this region.

5.2 Delegates and flight details

Most of the delegates left on 24 July and returned on 29 July with economy flights costing £579 per head. If delegates wanted to fly on dates other than those arranged by AstraZeneca, they would have to arrange and pay for flight changes and accommodation. As with Delhi, this was consistent with AstraZeneca meetings policy. Delegates booked their flights themselves through the AstraZeneca appointed travel agent. The agent was then reimbursed. Delegates were told that accommodation would only be booked on the conference dates so that if flights were booked outside of this period, they would have to bear the accommodation costs for the extra period. In addition, the travel agent was instructed to report to AstraZeneca any instances where delegates appeared to be booking family members on to the same flight. In these cases, of which there were approximately 10, AstraZeneca contacted the delegates involved to re-iterate that AstraZeneca would not bear any costs for those accompanying the delegates nor could they share conference accommodation or attend the meetings or meals. The travel instruction letter to the delegates was provided.

In total, AstraZeneca sponsored 105 delegates, of whom 19 left earlier and arrived back into the UK later than the pre-specified group times; 13 flew from the UK earlier, 2 later than the pre-specified group times and 11 flew back to the UK later and 18 earlier than the pre-specified group times. Of the 105 AstraZeneca delegates, approximately 15 were invited by SAF committee members on behalf of AstraZeneca.

The event was attended by 325 delegates, of which 105 were from the UK, 98 from India, 68 from Sri Lanka and 54 from other countries. Therefore the majority of delegates were from outside the UK and were largely from countries neighbouring Sri Lanka. Colombo, as a capital city with good transport links to other south Asian and non-south Asian countries, provided a convenient location in line with the other details ie theme of meeting, origin of presenters/experts etc.

Twelve AstraZeneca personnel attended, of whom seven were sales staff. The sales staff manned a promotional stand. No other company displayed a stand although AstraZeneca understood from SAF that personnel from other companies accompanied the delegates they had sponsored.

5.3 AstraZeneca closed satellite symposium

UK delegates attended an AstraZeneca sponsored closed satellite symposium entitled 'Get me well, keep me well!' AstraZeneca staff ensured that only UK delegates entered the meeting. The symposium took place on 25 July between 7 - 8.30pm and comprised presentations given by two independent UK psychiatrists and a workshop. Each of the speakers was provided with a copy of the AstraZeneca speaker briefing document valid in 2005 and an accompanying email that re-iterated the Code requirements. Dinner at the hotel followed after the symposium.

The symposium was patient centric and interactive and aimed to ask psychiatrists to think about what outcomes were most important for them and their patients. AstraZeneca reviewed all presentations beforehand to ensure the content was accurate, balanced and in line with internal compliance procedures. The presentations were an educational overview of a subject that was very much in line with the main theme of the conference. The presentations were provided.

AstraZeneca also organised 3 separate feedback and consultation meetings for some of the delegates who had attended the symposium. These meetings were organised and run by two members of the AstraZeneca medical department. Two of these meetings occurred on 26 July (11am – 1pm and 4pm – 6pm) and one on 27 July (2pm – 4pm). Approximately 10 delegates attended each and no payment was given for attendance. The meeting venue was a private meeting room in the conference hotel. A short presentation summarising data for AstraZeneca's product quetiapine was given, followed by a discussion where the doctors were asked to describe how useful they thought the presented data was in helping them to manage their patients. They could suggest what different types of data they would prefer. The presentations themselves were not now available but

they were drawn from approved slide sets. Minutes were kept (they were not now available). No sales or marketing personnel were present and no subsistence other than drinking water was provided.

5.4 Accommodation and hospitality costs

A letter to delegates regarding travel arrangements and logistics was provided which stated that congress associated accommodation would be sponsored and re-iterated AstraZeneca's policy on the attendance of spouses. A briefing letter to AstraZeneca personnel attending was provided and reminded them of the company's policy on the attendance of spouses

AstraZeneca met the hotel costs for the duration of the conference 24-29 July (an additional night was required to accommodate delegates' attendance on the last day of the meeting and therefore it was intended for all delegates to return to the UK on 29 July). Accommodation was arranged at a hotel in Colombo at a cost of £52 per head per night for 4 nights and £42 per head per night for one night. Those delegates who arrived earlier than 24 July or stayed later than 29 July had to make their own arrangements. The hotel was chosen for its large conference facilities capable of holding a meeting of this size. All sessions took place at the hotel. The standard of the hotel was not lavish or luxurious, was appropriate and in proportion to the meeting and justified.

Costs per head for subsistence dinner for each of five nights were budgeted at £10 per night and £3.20 for drinks with dinner. In addition, pre-dinner drinks of £4 per head for 4 nights were provided for 20 delegates selected by AstraZeneca personnel. Dinner was provided at the hotel for 4 nights and at a sports venue for the last night. The sports venue was not an international sporting venue and no sporting events were held at the time of the dinner. Dinner was served as a buffet on the stands of the ground and not in any hospitality suite. The costs associated with dinner were budgeted at £13.20 per night; they were not excessive, in proportion with the occasion, in line with what a delegate might expect to pay for themselves and therefore in line with AstraZeneca's own code of marketing and sales practice and the Code.

The actual costs incurred for accommodation, subsistence dinner and drinks was £70 per head per day.

AstraZeneca understood that SAF UK arranged for a Sri Lankan member of parliament and traditional Sri Lankan dancers to join dinner on one of the conference nights. AstraZeneca did not have prior knowledge of this event, did not initiate, pay for, promote or facilitate the logistics of any entertainment.

The record of actual spend for this meeting was provided.

Summary

AstraZeneca submitted that this was an educationally valid independent international scientific congress. AstraZeneca's arrangements in respect of travel, accommodation, subsistence and registration complied with the Code and AstraZeneca's external meetings policy

AstraZeneca therefore did not consider breaches of Clauses 2, 9.1 and 19.1 of the Code to have occurred.

6 SAF UK Regional Meeting, 7-8 July 2006, Birmingham

This large UK central region educational meeting was organised by the SAF and sponsored by AstraZeneca. The sponsorship covered the entire costs of the meeting including accommodation, meeting facilities, subsistence, speaker fees and travel expenses. No other pharmaceutical companies were involved.

6.1 Delegates and hospitality

AstraZeneca invited delegates to this meeting via the central region psychiatry sales force (invitation provided). This region spanned a central area of the UK that contained approximately a third of the total population. The invitation clearly stated that AstraZeneca took the Code seriously in letter and spirit and set out the company's policy on educational meetings.

Fifty-seven delegates, 11 speakers and 5 AstraZeneca personnel (including one sales representative) attended the meeting. Approximately a third of the delegates would have travelled for more than 1.5 hours. The three star hotel was chosen because of its central and convenient location; it was not a luxury or sporting venue and therefore could not be perceived as being the attraction for attending this meeting. AstraZeneca paid for accommodation at a cost per delegate per night of £158 for dinner and dinner beverages. These costs were appropriate and justified, not excessive, were in proportion to the meeting and secondary to its educational purpose. Costs were also in line with AstraZeneca's Code of Sales and Marketing practices, Meetings policy and the Code. Details of the actual spend for this meeting were provided.

6.2 Agenda

The agenda was compiled by AstraZeneca and SAF and was high in educational content with an hour and a half (6.30pm-8pm) on the Friday night followed by 4.75 hours on Saturday (9.30am-3.30pm), therefore providing 6.25 hours of education. Friday and Saturday were chosen to enable as many psychiatrists to attend as possible. Meetings of this duration held on weekdays were difficult for delegates to attend because of daytime commitments. Due to the duration of educational content and the need for attendees to undertake significant regional travel into Birmingham, all of which would have taken up more than a reasonable working day, an overnight stay was required, with content spread over 2 days. As stated before, the arrangements for dinner and accommodation were not such that they would have acted as the draw for this meeting. The dinner arrangements did not include entertainment of any kind.

AstraZeneca reviewed the presentations of all the speakers beforehand to ensure the content was accurate, balanced and in line with internal compliance procedures. All the speakers were independent health professionals. Copies of the presentations and delegate list were provided.

Summary

AstraZeneca submitted that in view of the valid educational content, significant regional travel required and the modest nature of the accommodation and subsistence, it did not believe that this meeting was in breach of Clauses 2, 9.1 and 19.1 of the Code

7 Forthcoming meeting in Dubai, UAE 1-6 December 2006 – 'Mental Health – From Early Recognition to Recovery'

AstraZeneca was planning to sponsor UK delegates to attend the above forthcoming recognised, independent international congress; over 300 delegates and speakers from all over the world were expected to attend of whom up to 80 would be AstraZeneca sponsored delegates from the UK.

The meeting and its agenda had been organised by SAF in collaboration with the WPA section on Psychiatry in Developing Countries and independently of AstraZeneca. The WPA was academic co-sponsor of the event.

A copy of the invitation and agenda was provided. The invitations had been formally approved in accordance with AstraZeneca compliance procedures and were very recently distributed to the field force to begin inviting delegates. All AstraZeneca delegates would be chosen and invited by AstraZeneca representatives and not by a third party. There had, as yet, been no acceptances and therefore a UK delegate list was not yet available.

AstraZeneca would pay the WPA registration fee (£200) for its delegates and the additional £150 SAF registration fee would be paid by the delegates themselves. SAF UK had already received more than 20 acceptances from delegates sponsored by other UK pharmaceutical companies.

7.1 Agenda

The agenda showed the meeting was planned to run over 3 full and 2 half days from 2 –6 December 2006. Delegates left the UK on 1 December and arrived in Dubai on the morning of 2 December.

Educational and scientific presentations and sessions accounted for a total of 22 hours of the meeting.

The speakers represented a truly international group with presentations given by those travelling from Pakistan, India, UK, Sri Lanka, USA, Australia, Thailand, Canada and Malaysia. Similarly, meeting delegates were expected mainly from South Asian countries but also from all over the world. Dubai was a logical and practical location for all speakers and delegates to travel to. Experience from the previous meetings in Lahore and Delhi had shown that many speakers and delegates from South Asian countries had experienced difficulties in obtaining a visa for travel from neighbouring countries ie India and Pakistan. Dubai therefore was an appropriate alternative location.

7.2 AstraZeneca closed satellite symposium

As part of the conference, AstraZeneca planned to run a closed symposium for UK delegates at the same venue as the main conference (see below) on 3 December. The general topic of this symposium would be atypical antipsychotics in bipolar disorder and schizophrenia. UK delegates would be separately invited to this event.

Both presentations were to be given by Canadian speakers. The slide content would be reviewed and approved by AstraZeneca beforehand. There were 2 hours of education which was clearly detailed in the meeting agenda/invitation. The meeting would be followed by a subsistence dinner at the same location. The arrangements did not include entertainment of any kind.

7.3 Accommodation and subsistence

AstraZeneca's UK delegates would stay at a hotel which was close to the airport and had good business facilities ie large meeting rooms and conference amenities. It was not a luxurious or sporting venue and therefore it was the educational content that was the principal attraction of this meeting. The per head cost of bed and breakfast accommodation was £160 per night. AstraZeneca had budgeted a maximum of £40 per head for dinner and £25 per head for lunch for each day although it was anticipated that the final costs might be less than this.

7.4 Flights

AstraZeneca would purchase and provide economy class flight tickets to its UK delegates. The flights would be scheduled such that they would land on the morning of the first day of the conference with delegates attending the start of the meeting that afternoon. The return flight would be on the same day that the conference finished. There was no flexibility available to delegates for travel outside of these dates and this was stated in the invitation. AstraZeneca had budgeted between £471 to £547 for economy class return flights for each anticipated delegate.

The meeting invitation clearly referred to AstraZeneca`s external meetings policy, with special reference to accompanying spouses.

7.5 Delegate costs

Other than the flights, accommodation, subsistence, local transfers and WPA registration costs detailed above, AstraZeneca was not bearing any other delegate costs for this meeting.

Arrangements were being made for eleven AstraZeneca staff to attend of whom four would be sales staff.

Summary

AstraZeneca submitted that the meeting was an educationally valid independent international scientific congress. The attendance of UK delegates was being sponsored by several UK pharmaceutical companies, including AstraZeneca. The printed agenda and AstraZeneca's arrangements for this meeting, with regard to travel, accommodation, subsistence and registration complied with the Code and AstraZeneca's external meetings policy. Therefore AstraZeneca did not consider this meeting to be in breach of Clauses 2, 9.1 and 19.1 of the Code.

Additional information

AstraZeneca stated that SAF had recently brought to its attention two evening events that would occur at this meeting:

a On the opening night of the congress (2 December) there would be dinner at the congress venue followed by a musical presentation reflecting the local culture. This musical event was offered free of charge by the hotel and accepted by the SAF. The first evening was also the evening of the inaugural ceremony and dinner as stated in the written agenda for this meeting. The cost per head for this dinner was budgeted at a maximum of £40 and in line with AstraZeneca policy for dinner costs.

b On the closing night (4 December) SAF had organised dinner for the delegates at an open-air restaurant in the desert that was approximately forty-five minutes' drive from the hotel. Dinner would be followed by a short musical presentation reflecting the local culture. Delegates would arrive back at the hotel by approximately 9.30pm. The cost per head was budgeted at a maximum of £40 per head and was in line with AstraZeneca policy for dinner costs.

AstraZeneca did not initiate, arrange, promote or logistically facilitate these planned musical presentations. Musical presentations and dinner at a venue separate to the main congress were not uncommon at international congresses on the opening and closing nights. Therefore AstraZeneca did not consider these arrangements breached Clauses 2, 9.1 or 19.1 of the Code.

Dinner on the remaining nights of the congress was at the congress venue and there was no music or entertainment of any kind.

Overlap of delegates attending the international meetings (Colombo, Delhi and Lahore).

The complainant had asserted that 'AstraZeneca again and again sponsored more or less same people to visit India and then Sri Lanka and Pakistan'.

However, AstraZeneca did not have a policy of inviting 'more or less same people' to international congresses. Indeed, after examining the delegate lists for all 3 of the above meetings, it was apparent that out of a total of 382 UK delegates that attended these meetings, 199 attended only 1 meeting, 71 attended 2 and 11 attended all 3.

The above numbers included all invitees, i.e. including organising/executive committee members who would be expected to attend most of the meetings.

Meeting in a Coventry Hotel

The complainant alleged that AstraZeneca met the expenses for a meeting at this hotel but did not specify a date. In order to be able to investigate further, AstraZeneca would require more information regarding this meeting.

Conclusions

AstraZeneca maintained that pharmaceutical sponsorship of such educational meetings was valid and facilitated opportunities for clinicians to share clinical experience from a range of healthcare environments. SAF and BIPA were independent organisations that AstraZeneca had worked with diligently to ensure that meetings arrangements were in line with the Code and AstraZeneca policies, and continued to remain so as the Code evolved.

PANEL RULING

The Panel noted the various meetings that AstraZeneca had sponsored. The Panel queried the relevance of some of the topics to UK practice.

The Panel noted the complaint was about the whole situation as well as the individual meetings. It appeared that SAF organised annual meetings and AstraZeneca was a major sponsor. Eleven doctors had been sponsored by AstraZeneca to each attend three meetings Colombo (July 2005), Delhi (February 2005) and Lahore (September 2004) in the space of ten months.

The Panel was generally concerned about the arrangements and impression given. It considered each event separately.

Coventry, 12-13 March 2004

The 2003 Code applied to this meeting.

The Panel noted that there was no agenda and no details of delegates or costs for the meeting. The only item provided regarding the arrangements for the meeting was an invitation letter which referred to the first West Midlands, South Asian Forum meeting. This was created by SAF. It appeared from this document that the business of the forum was dealt with on the Friday evening and the clinical and scientific programme was held on the Saturday morning. This was at odds with one of the presentation slides which stated that the business meeting ran from 9.30am to

10am on the Saturday morning. The clinical lectures ran from 10am until 12.45pm. A corporate presentation on AstraZeneca was given on the Friday evening.

The Panel was concerned that no details were available about the costs, the list of delegates or the final programme. The Panel did not consider that the length of the meeting (4.5 hours in total which according to AstraZeneca was 1.5 hours on Friday and 3 hours on Saturday morning) justified overnight accommodation as it could have easily been held over the course of a working day. The Panel did not know how far the delegates needed to travel to attend the meeting but noted that it was a regional meeting and so assumed that there would not be a large geographical spread of delegates. Furthermore the meeting was held in the West Midlands, an area of the country with an extensive road network.

The Panel noted that only a small number of delegates stayed on the Friday evening. The reason given by AstraZeneca was due to significant travel. The Panel queried this given the regional nature of the meeting. The Friday evening was not part of the meeting as such as most of the delegates had not attended. Given the length of the meeting on the Saturday it would have been possible to start the meeting a little later and for all the delegates to travel that day. On balance, the Panel did not consider that the overnight stay was justified and thus a breach of Clause 19.1 of the Code was ruled. The Panel did not consider that the circumstances warranted a ruling of a breach of Clauses 9.1 and 2.

Lahore, Pakistan, 16-20 September 2004

The 2003 Code applied to this meeting.

The Panel considered that from the programme the scientific/educational content was not unreasonable for sponsorship by a pharmaceutical company or for a pharmaceutical company to sponsor delegates to attend. The sessions ran generally from 9am – 5pm on each day. The programme stated that AstraZeneca was the sole sponsor for UK delegates via an unrestricted grant.

The educational grant was to cover economy air fare (budgeted at £575), five nights' stay at a hotel (£60 - £80 per night), subsistence (lunches and dinners), and WPA registration.

It was not necessarily unacceptable for UK health professionals to attend meetings outside the UK. The meeting was international with a proportion of delegates and speakers from outside the UK. If delegates wanted to travel outside 15 or 21 September then they were responsible for covering additional costs.

The Panel noted from AstraZeneca's submission that a live folk music presentation had been arranged by SAF. AstraZeneca stated that it had no part in the invitation, arrangement, promotion or logistical facilitation of this event.

The memorandum of understanding between AstraZeneca and SAF stated that the total cost per invited person was approximately £1100. The total educational grant from AstraZeneca was £55,000. All costs should be within this budget including AV costs, speakers (2 or 3) and any additional meeting costs. This would fund 50 to 55 delegates. The invitation to delegates referred to the need to comply with the Code.

Taking all the circumstances into account the Panel considered that the sponsorship by AstraZeneca for the meeting was not unacceptable and did not breach Clause 19.1 and thus no breach was ruled.

The Panel was, however, concerned to note that the memorandum stated that AstraZeneca representatives were to invite UK delegates from early 2004 'to reap benefit from beginning of year'.

The Panel did not consider that there had been breaches of Clauses 9.1 and 2 and ruled accordingly.

New Delhi, India, 3-6 February 2005

The 2003 Code applied to this meeting.

The Panel considered that from the programme the scientific/educational content was not unreasonable for sponsorship by a pharmaceutical company or for a pharmaceutical company to sponsor delegates to attend. There were two half day sessions and two full day sessions plus an AstraZeneca satellite symposium for UK delegates.

The educational grant (around £114,000) was to cover travel (average cost £672), 3 nights accommodation, subsistence and registration fee (£100) for 70 delegates.

It was not necessarily unacceptable for UK health professionals to attend meetings outside the UK. The meeting was international with a proportion of delegates and speakers from outside the UK.

The Panel noted that attendance at the conference necessitated a three night stay but 23 of those delegates sponsored by AstraZeneca (29%) travelled out earlier or returned later than the AstraZeneca appointed times with an average length of stay of 14 days. AstraZeneca submitted that the additional costs incurred by such changes were to be paid by delegates.

Taking all the circumstances into account the Panel considered that the sponsorship by AstraZeneca for the meeting was not unacceptable and did not breach Clause 19.1 and thus no breach was ruled.

The Panel did not consider that there had been breaches of Clauses 9.1 and 2 and ruled accordingly.

The Panel was concerned that delegates, including AstraZeneca staff, had taken the last day out of the conference to visit the Taj Mahal. This was not arranged or facilitated by AstraZeneca nor was it part of the programme but nevertheless the Panel considered that the participation of AstraZeneca staff

on such an outing which meant missing some of the sessions gave a poor impression. The Panel also noted that the trip took place on the day that return flights from Delhi (5.30pm) had been arranged.

Taking all the circumstances into account the Panel considered that the sponsorship by AstraZeneca for the meeting was not unacceptable and did not breach Clause 19.1 and thus no breach was ruled.

The Panel did not consider that there had been breaches of Clauses 9.1 and 2 and ruled accordingly.

Colombo, Sri Lanka, 24-28 July 2005

The 2003 Code applied to this meeting.

The Panel considered that from the programme the scientific/educational content was not unreasonable for sponsorship by a pharmaceutical company or for a pharmaceutical company to sponsor delegates to attend. There was one half day session and four full day sessions plus an AstraZeneca satellite symposium for UK delegates.

AstraZeneca funded travel and accommodation for 105 delegates covering flights (£579), 5 nights' accommodation, subsistence (total £350) and WPA registration fee (£136).

It was not necessarily unacceptable for UK health professionals to attend meetings outside the UK. The meeting was international with a proportion of delegates and speakers from outside the UK.

The Panel was again concerned that a number of delegates travelled outside the AstraZeneca appointed times but it was made clear that all additional costs were to be paid by delegates.

Taking all the circumstances into account the Panel considered that the sponsorship by AstraZeneca for the meeting was not unacceptable and did not breach Clause 19.1 and thus no breach was ruled.

The Panel did not consider that there had been breaches of Clauses 9.1 and 2 and ruled accordingly.

South Asian Forum UK Regional meeting, 7-8 July 2006, Birmingham

The 2006 Code applied to this meeting.

The Panel noted that AstraZeneca sponsored the entire costs of the meeting for 57 delegates. The educational part ran for 1.5 hours on the Friday evening and from 9.30am until 3.30pm on the Saturday (including refreshment breaks).

The Panel considered from the programme that the scientific/educational content (6.25 hours) was not unreasonable for sponsorship by a pharmaceutical company or for a pharmaceutical company to sponsor delegates to attend.

Taking all the circumstances into account the Panel considered that the sponsorship by AstraZeneca for the meeting was not unacceptable and did not breach Clause 19.1 and thus no breach was ruled.

The Panel did not consider that there had been breaches of Clauses 9.1 and 2 and ruled accordingly.

Dubai, 1-6 December 2006

The 2006 Code applied to this meeting.

The Panel considered that from the programme the scientific/educational content was not unreasonable for sponsorship by a pharmaceutical company or for a pharmaceutical company to sponsor delegates to attend. There were two half days and three full day sessions.

AstraZeneca was to sponsor 80 UK delegates to attend the meeting. It would pay flight costs (£471 - £574), accommodation (£160 per night), subsistence (maximum of £40 for dinner and £25 for lunch) and WPA registration fee (£200) ie approximately £1,670 per delegate.

It was not necessarily unacceptable for UK health professionals to attend meetings outside the UK. The meeting was international with a proportion of delegates and speakers from outside the UK.

The Panel was concerned that two musical presentations were included albeit that these were arranged independently of AstraZeneca by SAF and the hotel. In the Panel's view the musical presentations did not mean that the two dinners were wholly or mainly of a social nature.

The Panel considered that the subsistence offered appeared to be appropriate and not out of proportion to the occasion. It considered that the costs (around £1,670) were high and queried whether they were in line with the level that recipients would normally adopt when paying for themselves.

However, taking all the circumstances into account the Panel considered that the sponsorship by AstraZeneca for the meeting was not unacceptable and did not breach Clause 19.1 and thus no breach was ruled.

The Panel did not consider that there had been breaches of Clauses 9.1 and 2 and ruled accordingly.

Complaint received	**9 October 2006**
Case completed	**19 January 2007**

CASE AUTH/1899/10/06

EX-EMPLOYEE/THE MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY v ASTRAZENECA

Representative call rate frequency

The Medicines and Healthcare products Regulatory Agency forwarded a complaint from an ex-employee of AstraZeneca about representative call frequency targets in relation to the promotion of Casodex (bicalutamide). An AstraZeneca oncology sales and marketing booklet showing activity targets was provided, together with a company email explaining the call frequency targets for employees.

The complainant stated that the intensity of the campaign was such that main target doctors had to be called upon once a month. The carrot to achieve this frequency was the AZpiration scheme. Points for frequency could be exchanged for prizes, essentially an inducement to breach the Code.

During 2004 and the first 6 months of 2005 the oncology team was under extreme pressure to achieve, *inter alia*, (in 2004) 12 face to face calls a year on their main group of target customers. The complainant referred to two previous cases (Cases AUTH/1714/5/05 and AUTH/1737/7/05) which had involved AstraZeneca and call rates. Both complainants were anonymous and made comments about the culture at AstraZeneca.

If the carrot in the form of the AZpiration scheme failed to induce representatives into breaking the Code then a stick in the form of short term performance measures was threatened. This was viewed as the first step in a disciplinary process. This was a threat which could be used (formally and informally) and indeed was used to bully and harass representatives into achieving the frequency of 12 face to face calls. This amounted to harassment to break the Code.

The complainant noted that during 2004 and 2005 over 70% of the oncology team left AstraZeneca as they thought they were no longer working for an ethical company and were bringing the industry into disrepute. Many customers complained. Oncologists specialising in breast and prostate cancer would be targeted 36 times a year by the company.

The complainant alleged that AstraZeneca was able to break the Code for 18 months with regard to call frequency because a culture of bullying and harassment was introduced. The honest, open, supportive culture was changed to one where trust and confidence were deliberately destroyed with the appointment of two new senior executives. A witness statement from a separate matter stated 'There were presentations where everyone in the audience felt intimidated. Made to feel a bunch of failures, things were going to change, better toe the line'. A meeting in Ashby-de-la-Zouch in August 2004 was an example of this behaviour towards the breast oncology team.

The Panel noted that the complainant had referred, *inter alia*, to Case AUTH/1714/5/05 wherein it was alleged that AstraZeneca's psychiatry representatives were incentivised to see 90% of customers 16 times a year, 12 face to face meetings and 4 times at meetings. The Panel had noted, *inter alia*, that AstraZeneca had acknowledged that there might have been activity out of line with the supplementary information to the Code. This would be a consequence of following the campaign notes. Breaches of the Code had been ruled and no breach of Clause 2.

The Panel considered that the allegations about call rates and incentivisation were closely similar to those in Case AUTH/1714/5/05 and the rulings in that case applied here. Breaches of the Code were thus ruled. No breach of Clause 2 was ruled. In addition the Panel ruled a breach of the Code because the representatives' briefing material advocated a call rate that was likely to lead to a breach of the Code.

In relation to the allegations about comments made by a senior sales executive at a meeting the Panel noted that the company accepted that in hindsight the tone of the meeting was perhaps too critical. The slides provided did not appear unreasonable; however there were no speaker notes nor was a transcript of the meeting available. It was thus not possible to determine whether what had been said at the meeting amounted to a breach of the Code. No breach was ruled.

The Medicines and Healthcare products Regulatory Agency (MHRA) forwarded a complaint from an ex-employee of AstraZeneca UK Limited, about representative call frequency targets in relation to the promotion of Casodex (bicalutamide). An AstraZeneca oncology sales and marketing booklet showing activity targets was provided together with a company email explaining the call frequency targets for employees.

COMPLAINT

The complainant stated that the intensity of the campaign was such that frequency of calling on their main target doctors of once a month was demanded. The carrot to achieve this frequency was the AZpiration scheme. Points for frequency could be exchanged for prizes, essentially an inducement to breach the Code.

During 2004 and the first 6 months of 2005 the

oncology team was under extreme pressure to achieve metrics which included (in 2004) 12 face to face calls a year on their main group of target customers. Representatives tried to raise their concerns about achieving these metrics and staying within the Code via their union representative. Concern was raised at all levels of management. The representatives did not receive any advice. It was mentioned at a management group that they were breaching the Code. Their concerns were not escalated as a management team because they were in fear of losing their jobs.

The complainant noted two cases involving AstraZeneca (Cases AUTH/1714/5/05 and AUTH/1737/7/05) had involved call rates. Both complainants were anonymous stating '… if one raised this with AstraZeneca, it would not make any difference and would be a career-limiting move' and 'This fear culture also prevented the complainant from revealing his/her identity. Reprisals would be severe and covert'. The Panel had queried whether it was appropriate to give representatives targets to meet objectives over which the Panel considered they should have little influence.

If the carrot in the form of the AZpiration scheme failed to induce representatives into breaking the Code then a stick in the form of short term performance measures was threatened. This was viewed as the first step in a disciplinary process. This was a threat which could be used (formally and informally) and indeed was used to bully and harass representatives into achieving the frequency of 12 face to face calls. This amounted to harassment to break the Code.

During 2004 and 2005 over 70% of the oncology team left AstraZeneca as they thought they were no longer working for an ethical company and were bringing the industry into disrepute. Many customers complained. Oncologists specialising in breast and prostate cancer would be targeted 36 times a year by the company (12 x Faslodex, 12 x Arimidex and 12 x Casodex/Zoladex).

The complainant alleged that AstraZeneca was able to break the Code for 18 months with regard to call frequency because a culture of bullying and harassment was introduced. The honest, open, supportive culture was changed to one where trust and confidence were deliberately destroyed from January 2004 with the appointment of two new senior executives. A witness statement for a separate matter stated 'There were presentations where everyone in the audience felt intimidated. Made to feel a bunch of failures, things were going to change, better toe the line'. A meeting in Ashby-de-la-Zouch in August 2004 was an example of this unwanted behaviour towards the breast oncology team. The company should have a transcript or tape of the meeting.

The complainant claimed to have a wealth of documents to back these allegations.

When writing to AstraZeneca the Authority asked it to respond in relation to Clauses 2, 9.1, 15.4 and 15.9 of the 2003 edition of the Code.

RESPONSE

AstraZeneca explained that in early 2006 a member of the urology sales team had made various allegations against the company. Some of these matters were the subject of an ongoing legal dispute. One of the allegations, AstraZeneca believed, formed the basis of this complaint ie that call frequency targets set in 2004 and early 2005 were in breach of the Code and that there was a culture of inducement or harassment to breach the Code in that regard.

AstraZeneca noted that in May 2005 it had received a complaint (Case AUTH/1714/5/05) the essence of which was that the company was setting call frequency rates so high as to induce a breach of the Code and, in particular, requiring its representatives to over call on customers; that representatives were actively incentivised to breach the Code under the AZpiration scheme; that failure to comply with targets would adversely affect pay and promotion prospects and that raising concerns would be career-limiting. Breaches of Clauses 15.4 and 9.1 of the Code were ruled.

In July 2005 AstraZeneca received another complaint (Case AUTH/1737/7/05) that a senior executive had encouraged overcalling on customers in breach of the Code, and that a 'fear culture' existed within AstraZeneca. AstraZeneca was ruled in breach of Clauses 15.9 and 9.1 of the Code.

In both cases AstraZeneca accepted the rulings and put in place a comprehensive and detailed package of measures details of which it provided. In neither the investigations themselves nor the Panel's rulings were the allegations concerning a 'fear culture' at AstraZeneca supported.

The basis of the current complaint (Case AUTH/1899/10/06) was the rulings from Cases AUTH/1714/5/05 and AUTH/1737/7/05. Indeed, these were expressly referred to by the complainant. However, for clarity the following specific allegations, all relating to 2004 and early 2005, were made:

- Once a month calling on target doctors and 12 face to face calls on target customers.
- AZpiration scheme – points for frequency essentially an inducement to break the Code.
- Concerns raised with union representatives and at all levels of management and no advice given.
- Representatives threatened with disciplinary action if they failed to achieve the frequency targets and a general culture of bullying and harassment.
- Presentation by a senior sales executive in August 2004 which intimidated the audience.

In AstraZeneca's view the current complaint clearly concerned a matter closely similar to one which had been the subject of a previous adjudication and so the Director should exercise her discretion under Paragraph 5.1 of the Constitution and Procedure and not proceed with it.

AstraZeneca's reasons for not proceeding were:

- No new evidence had been adduced by the complainant.

There were only two points of substance that were different with the current case and Cases AUTH/1714/5/05 and AUTH/1737/7/05. The first was that Case AUTH/1714/5/05 focused on the AstraZeneca psychiatry team rather than the oncology sales team. However, in practice, the investigations conducted by AstraZeneca, the responses made to the Authority and the remedial action taken by the company did not focus only on psychiatry. The second difference related to the presentation in August 2004 and AstraZeneca's separate response to this was set out below. However, AstraZeneca believed the complaint about this meeting did not relate to an actual or potential Code breach and therefore was not something the Authority would ordinarily investigate.

- Passage of time or change in circumstances raised doubts as to whether the same decision would be made in respect of the current complaint.

The substance of the complaint related to fundamentally the same activities and materials as the previous cases. It was not possible to see how the passage of time or change in circumstances could therefore have any bearing on the conclusions reached. One element of this complaint was that concerns were raised with union representatives and at all levels of management but that no advice was given. This lack of clarity had however already been acknowledged as part of the response to Case AUTH/1714/5/05 where the company accepted that there might have been activity out of line with the requirements of the supplementary information to Clause 15.4 and in the response to Case AUTH/1737/7/05 where it was stated that, '[the senior executive] was open with the fact that he had not [in the past] provided clarity around achieving call frequency within the ABPI Code of Practice. This was followed by explicit instruction on how this could be achieved'.

- The complaint covered matters similar to those in a decision of the Panel, which was not appealed.

AstraZeneca took corporate governance and compliance with the Code very seriously as restated in various submissions. It did not appeal the previous adjudications for this reason. AstraZeneca therefore felt that it would be inequitable to prejudice its position now by proceeding with the current case simply due to its decision not to appeal the previous rulings. The potential danger of following such a course would be that companies would be compelled to appeal all decisions to preserve their arguments under Paragraph 5.1.

With regard to the complainant's statement that during 2004 and 2005 over 70% of the oncology team left AstraZeneca as they thought they were no longer working for an ethical company and bringing the industry into disrepute, AstraZeneca noted that records showed that the number leaving the oncology sales force in 2004 was similar to the attrition rates across the business. More people (far below 70%) left in 2005 but this followed a significant reorganisation of the team in 2004. In addition, no-one in the oncology team gave, as a reason for leaving, 'no longer working for an ethical company and bringing the industry into disrepute', and no leavers stated they were leaving due to a culture of 'bullying and harassment'. However, approximately 10% of leavers stated they were 'unhappy with management style' and 20% stated they were 'unhappy with the environment'. Neither of these reasons were unusual considering the realignments ongoing in the oncology teams.

AstraZeneca noted that the Authority had asked it to respond to the allegations made but it believed that this case should not proceed pursuant to Paragraph 5.1 of the Constitution and Procedure, for the reasons set out above. It should also be considered that all of the remedial action already undertaken by AstraZeneca in response to the previous cases would address the issues raised in this complaint, some of which were outlined below.

Measures had included:

- The sales force incentive scheme was no longer linked to frequency of calling on individual customers. The current incentive scheme was based on sales measures such as market share or volume growth. The only customer facing metric for the oncology sales team was that of attendance of customers at meetings and this constituted a small proportion of the total possible bonus (<20%). Total call volume was a metric option used for the primary care sales force and this constituted a small proportion of the total possible bonus (<20%).
- All representatives were comprehensively trained on the Code.
- All internal meetings involving representatives now included five mandatory slides summarising key Code's requirements. The requirement that only three unsolicited calls per representative, per customer, per year were allowed was explicitly highlighted.
- AstraZeneca had developed an emphasis on call quality, over quantity. This was reflected in its incentive schemes as well as in the delivery of presentations by the company's senior management.
- Activity targets had been revised to ensure that no customer received more than 3 unsolicited calls per year and all calls were logged within a database, including details of whether the call was solicited or unsolicited.

With regard to corporate culture the company had:

- Established a corporate reputation group and increased emphasis on an open, honest culture throughout the business. The Code and corporate compliance had a high profile within the company with a variety of measures instituted since the Code breaches in 2005.
- In mid-2005 all managers attended a meeting on compliance and company vision during which the details of the breaches of the Code in Case

AUTH/1714/5/05 were shared. These messages were cascaded to the sales force in subsequent meetings. A renewed vision based on 'Winning the Right Way' was developed together with four strategic cornerstones to drive a culture of intelligent compliance.
- All staff were formally trained on the Code and the AstraZeneca Code of Sales and Marketing Practice. All new starters had to read, pass a small test and acknowledge that they would abide by all AstraZeneca's codes within 1 month of joining the company. A record was kept of all non-compliers and reported monthly in the director's governance report so that the directors could investigate if individuals required further support.
- In early 2006, when the new Code was launched, all representatives received a CD Rom and guidance booklet highlighting the main changes to the Code.
- Annually, all representatives renewed their commitment to AstraZeneca's policies (including the Code) and a register was kept of their recommitment.
- All staff could raise concerns about compliance in confidence at any time through several different channels including contacting the line manager, another senior manager within the organisation, the UK compliance officer or at corporate headquarters or employee relations.

With regard to the presentation in August 2004 where the complainant alleged that everyone in the audience felt intimidated, AstraZeneca explained that during 2004 the oncology team was significantly restructured. There were several new managers appointed. In addition, in 2004, a new selling model was introduced to improve in-call performance. These organisational changes unsettled some members of the oncology sales force, especially those who had been working under the previous management team and structure for many years.

In August 2004, the AstraZeneca breast team held a full-day meeting in Ashby-de-la-Zouch. This meeting was not recorded, so no transcript was available of what was said, but AstraZeneca had established the following:

- The meeting ran from approximately 10am until 3.30pm.
- Attendees included all breast sales representatives, oncology sales managers, members of the head office breast cancer brand team and relevant staff from the learning and development team. The urology sales force was not involved.
- The purpose of the meeting was to share the results of some market research that had evaluated the impact of the breast sales team interactions with their target customers.
- The meeting included a presentation which overviewed the poor performance of the team with respect to recall of key messages by their target customers. This was to challenge and motivate a group of talented, well-paid representatives to raise their level of performance.
- The focus of the presentation was on the quality of the interactions, not on the frequency of calls on individual customers.
- The day also included small group workshops to brainstorm potential solutions which were led by sales managers.
- The day included validation of the representatives against the AstraZeneca selling model to evaluate the standard of the representatives. This was led by the learning and development function, with support by sales managers.

From the accounts of attendees it was evident that the meeting held in August 2004 had not entirely met its objective of challenging and motivating the breast oncology sales force. In hindsight, the tone of the meeting was perhaps too critical. However, the meeting focussed on the quality of interactions and on customer message recall in order to improve performance, not on the issues surrounding the frequency of calls on individual customers.

PANEL RULING

The Panel noted that the complainant had referred, inter alia, to Case AUTH/1714/5/05 wherein it was alleged that AstraZeneca's psychiatry representatives were incentivised to see 90% of customers 16 times a year, 12 face to face meetings and 4 times at meetings. The Panel had noted, *inter alia*, that AstraZeneca had acknowledged that there might have been activity out of line with the supplementary information to Clause 15.4 of the Code. This would be a consequence of following the campaign notes. Thus the Panel had ruled a breach of Clause 15.4. The Panel considered that AstraZeneca had not maintained high standards. A breach of Clause 9.1 had been ruled. The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was reserved as a sign of particular censure.

The Panel considered that the allegation in the present complaint, Case AUTH/1899/10/06, about call rates and incentivisation was closely similar to those considered in Case AUTH/1714/5/05. AstraZeneca had invited the Director to exercise the discretion given to her under Paragraph 5.1 of the Constitution and Procedure to decide not to proceed with Case AUTH/1899/10/06. The Panel noted that Paragraph 5.1 of the Constitution and Procedure provided, *inter alia*, that if a complaint concerned a matter closely similar to one which had been the subject of a previous adjudication the Director should normally allow it to proceed if it was not the subject of an appeal to the Appeal Board. Case AUTH/1714/5/05 had not been subject to an appeal to the Appeal Board and the Director had thus decided to allow the present case to proceed.

The Panel was thus obliged to consider the matter. The Panel considered that the allegations about call rates and incentivisation were closely similar to those in Case AUTH/1714/5/05 and the rulings in that case applied here. Breaches of Clauses 9.1 and 15.4 were thus ruled. No breach of Clause 2 was ruled. In addition the Panel ruled a breach of Clause 15.9;

the representatives' briefing material advocated a call rate that was likely to lead to a breach of the Code.

In relation to the allegations about comments made by a senior executive at a meeting the Panel noted that the company accepted that in hindsight the tone of the meeting was perhaps too critical. The slides provided did not appear unreasonable; however there were no speaker notes nor was a transcript of the meeting available. It was thus not possible to determine on the balance of probabilities whether what had been said at the meeting amounted to a breach of Clauses 15.4 or 15.9; no breach of these clauses was accordingly ruled.

Complaint received	**11 October 2006**
Case completed	**19 January 2007**

CASE AUTH/1910/11/06

SANOFI PASTEUR MSD v GLAXOSMITHKLINE

Cervical cancer disease awareness campaign

Sanofi Pasteur MSD complained about GlaxoSmithKline's field based cervical cancer disease awareness team (CCDAT) alleging that the existence and activities of CCDAT breached, *inter alia*, Clause 2 of the Code.

Sanofi Pasteur MSD and GlaxoSmithKline had each developed prophylactic human papillomavirus (HPV) vaccines. Sanofi Pasteur MSD's vaccine, Gardasil, targeted four HPV types: 6, 11, 16 and 18 and GlaxoSmithKline's candidate vaccine targeted HPV types: 16 and 18. Gardasil was launched in the UK in October 2006. GlaxoSmithKline's candidate vaccine was not licensed.

Sanofi Pasteur MSD was concerned that a Pharmaceutical Field advertisement sought area managers and representatives for the CCDAT to 'shape the future for women in the UK'. The advertisement explained that the successful candidates would, by providing disease awareness education to key primary care health professionals within the territory, develop the understanding of cervical cancer and then at launch of the vaccine be responsible for the sales performance on the territory and account management of customers. A proven track record in sales, with excellent negotiation and influencing skills was required. This implied that the pre-launch disease awareness phase would be an opportunity to develop a network of customers, to be leveraged at launch, in order to achieve sales performance on each territory.

Sanofi Pasteur MSD accepted that provision of information on health and disease by companies could be non-promotional. However, if the information related to a disease area of interest to a particular company, it would be considered promotional and within the scope of the Code, even if no product was mentioned. In addition, the disease awareness and commercial objectives of the team were so closely intertwined that it was unrealistic to expect sales professionals to separate the two.

Sanofi Pasteur MSD provided copies of some of the materials used which included a leavepiece, a brochure and exhibition panels. These followed a common theme with messages about the burden of cervical cancer, the cervical screening programme and the link with HPV infection. All referred to immunity, stating 'Previous infection with HPV may not provide sufficient immunity to prevent another infection'.

The combination of the mention of HPV types 16 and 18, reference to immunity (which would be associated with vaccination) and the fact that GlaxoSmithKline was one of the largest vaccine suppliers in the UK made it highly likely that this material would lead to questions about HPV vaccination and GlaxoSmithKline's candidate vaccine.

The activities of the CCDAT were having the effect of soliciting questions to GlaxoSmithKline about vaccines that it had an interest in, but whose product was currently unlicensed. No amount of training on how to deflect such questions or refer them to the medical department could detract from that. Furthermore, questions being prompted by the concerted activities of the CCDAT could not be considered truly unsolicited and therefore the responses provided, even if under the responsibility of the medical department, could be considered promotional.

Sanofi Pasteur MSD considered it was impossible for the team's activities to be non-promotional.

The Panel noted that the Code permitted certain activities prior to the grant of the marketing authorization. The legitimate exchange of medical and scientific information during the development of a medicine was not prohibited providing that any such information or activity did not constitute promotion prohibited by the Code.

In the Panel's view the closer to the grant of the marketing authorization for a product the more difficult it was to argue that activities were a legitimate exchange of medical and scientific information during the development of a medicine.

The definition of promotion did not include replies made in response to individual enquiries from members of the health professions or appropriate administrative staff or in response to specific communications from them whether of enquiry or comment, including letters published in professional journals, but only if they related solely to the subject matter of the letter or enquiry, were accurate and did not mislead and were not promotional in nature. This exemption applied to unsolicited enquiries only ie whereby companies responded to an enquiry having done nothing to prompt it. In answering an unsolicited enquiry a company could offer to provide further information. If the enquirer subsequently requested additional information this could be provided and would be exempt from the Code provided it met the requirements of the exemption. Information relating to human health or diseases were also exempt from the definition of promotion provided there was no reference either direct or indirect to specific medicines.

In the Panel's view it was not necessarily unacceptable for companies to have employees

focussing on the provision of information prior to the grant of the marketing authorization. The arrangements and activities of such employees had to comply with the Code. Such employees should be comprehensively briefed about the Code. The area was difficult and companies needed to ensure that the arrangements and activities were very carefully controlled and managed.

The Panel noted GlaxoSmithKline's submission that the role of CCDAT was to educate relevant health professionals about the burden of cervical cancer and precancerous lesions, the causal role of oncogenic HPV in cervical cancer and the importance of the screening programme.

A detail aid 'Cervical cancer - a major health issue for women' discussed the incidence and cause of cervical cancer and the success of cervical screening in the UK and stated 'Previous infection with HPV may not provide sufficient immunity to prevent another infection'. The brochure concluded with 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer' above 'Cervical cancer prevention for all women' in logo format. Identical statements appeared in a smaller, abridged leavepiece which bore an identical title. Banner headlines on each of the three exhibition panels provided, discussed either the cause, incidence and/or burden of cervical cancer, one stating that '… previous infection with HPV may not provide sufficient immunity to prevent another infection'. Each concluded with the strapline 'Regular cervical screening is vital in the fight against cervical cancer'. A smaller exhibition panel simply read 'Cervical cancer prevention for all women' with the GlaxoSmithKline logo.

The representatives' briefing document, 'Cervical Cancer Disease Awareness Campaign', provided detailed information on the discussion points in the detail aid and leavepiece described above. The need to comply with the Code was highlighted. Representatives were told that '… it is possible that [health professionals] may ask about HPV vaccination and/or GlaxoSmithKline's vaccine in development, which must not be discussed under any circumstances'. A section headed 'To watch out for' gave three model answers. Firstly, to use if health professionals asked about why the representatives were talking about cervical cancer and not selling a product. Secondly, to use after Sanofi Pasteur MSD's product has been launched. If asked specifically about GlaxoSmithKline's candidate HPV vaccine representatives were advised to state that the purpose of the visit was to discuss cervical cancer disease awareness and not specific products and that GlaxoSmithKline's medical information team would be able to assist with any specific product enquiries. The representatives' disease awareness training material did not discuss medicines; it concluded with a section on screening and diagnosis.

The Panel considered that the material would encourage discussion about cervical cancer. This was not necessarily unacceptable so long as the material did not solicit questions about a specific medicine and that any discussion complied with the Code. The references to previous infection not providing sufficient immunity to prevent another infection might solicit general questions about vaccination. Whilst the Panel noted GlaxoSmithKline's explanation that such references emphasised the need for continued regular screening in older woman who remained sexually active the Panel did not consider that this explanation was made clear in any of the materials. Nonetheless, the overall emphasis of each item was on the burden and cause of disease and the need to ensure access to a successful screening programme. The Panel considered that the unqualified statement 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer' would encourage doctors to ask about GlaxoSmithKline's role in prevention. The Panel noted that the model answers all indicated that the representative should state that the purpose of their visit was to discuss cervical cancer disease awareness, and not specific products.

Overall the Panel considered that the material and activities of the representatives did not identify, directly or indirectly, a specific medicine such that GlaxoSmithKline's medicine was being promoted prior to the grant of its marketing authorization. Nor did the material solicit enquiries about GlaxoSmithKline's forthcoming product. The Panel ruled no breach of the Code. This was appealed by Sanofi Pasteur MSD.

The Appeal Board noted that the recruitment advertisement that appeared in the April 2006 issue of Pharmaceutical Field, a journal aimed at sales professionals, stipulated that candidates for the position of representatives should have a proven track record in sales, with excellent negotiation and influencing skills. The advertisement referred to delivering a focussed disease awareness campaign and then implementing the launch of the vaccine in early 2007. The Appeal Board considered that whilst a sales background was not necessarily unacceptable it was, however, consequently important that the company was especially careful about the arrangements and activities given a representative's natural tendency to sell. The Appeal Board also noted the company representatives' submission that approximately 25% of the CCDAT team was recruited from a non-sales position.

The Appeal Board noted GlaxoSmithKline's submission about the CCDAT non promotional role and training but was nonetheless concerned about the scale of the activity; there were 65 members of the CCDAT operating throughout the UK, targeting potential prescribers. It was likely that most of the CCDAT would promote GlaxoSmithKline's vaccine to the same group of prescribers once the product had received its marketing authorization.

The Appeal Board did not accept the GlaxoSmithKline representatives' position that the primary purpose of the CCDAT and materials was to increase screening rates. The company

representatives had explained that the targeted practices were those with large numbers of female patients registered and not those with low uptake of cervical screening.

The Appeal Board noted that HPV types 16 and 18 were responsible for 71.5% of cervical cancers. Fifteen of the 100 HPV types identified could cause cervical cancer. The Appeal Board was concerned about the overall emphasis of the detail aid on HPV types, particularly oncogenic HPV types 16 and 18, given the stated primary objective of the campaign to increase screening levels. The Appeal Board considered that this objective could be achieved without such emphasis. In particular three out of four bullet points on the final page of text (page 13), which the Appeal Board inferred summarized the key take-home message of the detail aid, referred to oncogenic HPV types 16 and 18 and/or HPV infection. There was no mention of screening. Further the references to and undue emphasis on only oncogenic HPV types 16 and 18 could only relate to a specific medicine; GlaxoSmithKline's forthcoming vaccine. (The currently available vaccine Gardasil, was indicated for HPV types 6 and 11 as well as oncogenic HPV types 16 and 18.) The page also stated that 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer'. The company explained that the support referred to comprised discussion with health professionals by members of the CCDAT about the importance of screening, sponsorship of educational meetings and the provision of patient leaflets. The Appeal Board did not have copies of the patient leaflets before it.

Overall the Appeal Board considered that the cumulative effect of the arrangements amounted to promotion of a product prior to the grant of its marketing authorization. A breach of the Code was ruled. It thus considered that the arrangements would bring discredit upon and reduce confidence in the pharmaceutical industry; a breach of Clause 2 was ruled.

Sanofi Pasteur MSD Ltd complained about the activities of a field based team of GlaxoSmithKline UK Ltd known as the cervical cancer disease awareness team (CCDAT).

COMPLAINT

Sanofi Pasteur MSD alleged that the existence and activities of CCDAT breached Clauses 2 and 3.1 of the Code.

Sanofi Pasteur MSD explained that it and GlaxoSmithKline had each developed prophylactic human papillomavirus (HPV) vaccines. Sanofi Pasteur MSD had developed Gardasil, which targeted four HPV types: 6, 11, 16 and 18 and GlaxoSmithKline had developed a candidate vaccine which targeted two HPV types: 16 and 18. HPV was the essential cause of cervical cancer, as well as being responsible for various other diseases.

Gardasil was launched in the UK on 17 October 2006. GlaxoSmithKline's candidate vaccine was not licensed.

Recruitment of CCDAT

The advertisement placed by GlaxoSmithKline in the April 2006 issue of Pharmaceutical Field sought area managers and representatives to 'shape the future for women in the UK'. The opening paragraph read:

'As one of the world's leading research-based pharmaceutical and healthcare companies, GlaxoSmithKline develops new products with the objective to enable people to do more, feel better and live longer. We are currently making that vision a reality by preparing to launch a revolutionary new vaccination against human papillomavirus (HPV), the cause of cervical cancer. So by joining us at this crucial time, you'll have the chance to shape the development of this new opportunity and then lead the launch of the brand on your territory. This is a unique career opportunity in a new field of women's health and cancer prevention.'

The advertisement worried Sanofi Pasteur MSD for a number of reasons:

1 The opening paragraph, quoted above, made it clear that the representatives would, in the pre-launch phase, shape the future of vaccination against HPV and then lead the launch of GlaxoSmithKline's candidate vaccine on their territory.

2 The second and third paragraphs stated that the disease awareness campaign would be directed at primary care health professionals, many of whom were prescribers.

3 The third paragraph stated:

'By providing disease awareness education to key Primary Care Health Care Professionals within your territory, you will initially be focussed on developing the understanding of cervical cancer. At launch of the vaccine you will be responsible for the sales performance on your territory and account management of your network of customers. You will need a proven track record in sales, with excellent negotiation and influencing skills.'

This implied that the pre-launch disease awareness phase would be an opportunity to develop a network of customers, to be leveraged at launch, in order to achieve sales performance on each territory. Furthermore, it was a requirement that, although operating as a disease awareness team, all representatives were required to come from a sales background.

It was therefore clear from the advertisement that sales professionals were being recruited to prepare their territories through a disease awareness campaign in readiness for the future launch of GlaxoSmithKline's candidate HPV vaccine. Those same representatives would be responsible for the sales success of the vaccine on those same territories, with the very same

customers. Sanofi Pasteur MSD accepted that provision of information on health and disease by companies could be non-promotional. However, it believed that, if the information related to a disease area of interest to a particular company, it would be considered promotional and within the scope of the Code, even if no product was mentioned. In addition, the disease awareness and commercial objectives of the team were so closely intertwined that it was unrealistic to expect sales professionals to separate the two.

In previous correspondence Sanofi Pasteur MSD had referred GlaxoSmithKline to Cases AUTH/1346/7/02, AUTH/1559/3/04 and AUTH/1560/3/04. In correspondence, GlaxoSmithKline had informed Sanofi Pasteur MSD that 25% of the team were recruited from a non-sales background within GlaxoSmithKline.

Activities of CCDAT and materials used

In correspondence GlaxoSmithKline had stated the objective of the CCDAT was:

> '…to increase awareness and understanding amongst relevant health professionals of the burden associated with Cervical Cancer, the causal role of oncogenic Human Papilloma Virus (HPV) and the importance of regular cervical screening.'

Sanofi Pasteur MSD was aware from feedback from the field that the CCDAT was active in surgeries and at local meetings, interacting on a one-to-one basis with general practitioners and practice nurses. Sanofi Pasteur MSD provided copies of some of the materials used by the team, which included a leavepiece (20959476 CER/LVP/06/27063/1 August 2006), a brochure (CER/DAP/06/26681/1 July 2006) and exhibition panels.

The materials followed a common theme with messages about the burden of cervical cancer, the cervical screening programme and the link with HPV infection. All three pieces of material also referred to immunity, stating:

> 'Previous infection with HPV may not provide sufficient immunity to prevent another infection.'

The combination of the mention of HPV types 16 and 18, reference to immunity (which many primary care professionals would associate with vaccination) and the fact that GlaxoSmithKline was one of the largest vaccine suppliers in the UK made it highly likely that this material would lead to questions about HPV vaccination and GlaxoSmithKline's candidate vaccine.

Bearing in mind the stated objective of the CCDAT, Sanofi Pasteur MSD noted the messages chosen for the three exhibition panels. The first carried a message about the burden of cancer and precancerous lesions; the second, a message about oncogenic HPV infection; the third, a message about immunity. Cervical screening was referred to only in rather small text at the bottom of each panel.

Sanofi Pasteur MSD submitted photographs of the exhibition stands taken at a cervical screening update meeting attended by approximately 50 practice nurses. The meeting was sponsored by industry and five companies including GlaxoSmithKline had stands. GlaxoSmithKline had confirmed in correspondence that this was being replicated elsewhere in the country.

Requests for information

It was highly likely that a GlaxoSmithKline representative, even if deemed non-promotional, who discussed cervical cancer and HPV would prompt questions about vaccination, and hence GlaxoSmithKline's candidate vaccine. Feedback from the field indicated that this was indeed the case and the possibility was acknowledged by GlaxoSmithKline in its letter dated 19 October 2006, which stated:

'It was acknowledged that HPV vaccination might be raised by some healthcare professionals (HPs) as a result of the disease awareness programme. However, these non promotional representatives have been thoroughly trained and assessed on how to handle potential questions from HPs about this topic specifically in order to prevent any discussion of unlicensed products. If a HP is persistent in their request for information regarding HPV vaccination the disease awareness team has been instructed to refer that HP to our medical information department.'

It was clear therefore that the activities of the CCDAT were having the effect of soliciting questions to GlaxoSmithKline representatives about vaccines that it had an interest in, but whose product was currently unlicensed. No amount of training on how to deflect such questions or refer them to the medical department could detract from that. Furthermore, questions being prompted by the concerted activities of the CCDAT could not be considered truly unsolicited and therefore the responses provided, even if under the responsibility of the medical department, could be considered promotional.

Summary

In the case of the CCDAT, Sanofi Pasteur MSD considered it was impossible for the team's activities to be non-promotional because:

1 Potential prescribers were targeted through one-to-one contact, either in surgeries or at meetings.
2 Awareness of vaccines against cervical cancer was high amongst health professionals.
3 GlaxoSmithKline was one of the largest vaccine suppliers in the UK.
4 The activities of the team were bound to, and had, prompted questions about vaccination, and hence GlaxoSmithKline's candidate HPV vaccine.

In Sanofi Pasteur MSD's view, the existence and activities of the CCDAT breached Clause 3.1 of the Code. The manner in which the team was recruited, the inexorably close ties between disease awareness and future brand success, and the materials and tactics being employed inevitably promoted a product prior to receipt of its marketing authorization. None of the exemptions relating to advance notification of new

products applied to the target audience of primary health professionals.

Furthermore, Sanofi Pasteur MSD was concerned that this represented a new and worrying precedent in the activities of field-based representatives: disease awareness directed one-to-one at future prescribers pre-launch to be followed by traditional promotion post-launch. As well as breaching Clause 3.1 in the pre-launch phase, Sanofi Pasteur MSD believed that the prominence of the CCDAT, the inexorable link between disease awareness and future commercial promotional objectives, and the extent of its activities brought discredit upon, and reduced confidence in, the pharmaceutical industry as a whole and thus breached Clause 2.

RESPONSE

GlaxoSmithKline stated that it had had the spirit and letter of the Code in mind when it had recruited the CCDAT and planned its activities. As such, it was confident that the existence of this non-promotional team and its activities complied with the Code.

The causal role of the oncogenic (cancer causing) HPV in cervical cancer was well documented. However, several recent publications had highlighted that knowledge about oncogenic HPV and its role in this disease was very limited amongst women and that further education for health professionals in this area had been called for. The CCDAT was established to help address this genuine knowledge gap. The CCDAT was launched by GlaxoSmithKline on 4 September 2006 with the clear objective to educate relevant health professionals about the burden of cervical cancer and precancerous lesions, the causal role of oncogenic HPV in cervical cancer and the importance of the screening programme. As such, GlaxoSmithKline strongly refuted a breach of Clause 3.1 and, thus, Clause 2 of the Code.

It was incorrect to assume that it was not possible for non-promotional disease awareness representatives to undertake education in a disease area in which the company had an interest. As Sanofi Pasteur MSD was aware, these activities were permitted under the Code, and as would be noted in correspondence with Sanofi Pasteur MSD, GlaxoSmithKline maintained that the non-promotional representatives of the company (comprising the CCDAT) were permitted to call directly on health professionals.

Sanofi Pasteur MSD referred to Cases AUTH/1346/7/02, AUTH/1559/3/04 and AUTH/1560/3/04 to support its allegations. GlaxoSmithKline was aware of these previous rulings and noted that breaches of Clause 3.1 were demonstrated in each case. However, there were no similarities between those cases and the CCDAT activities. Clear deviation from genuine disease awareness campaigns occurred in each of the cases cited, with representatives either subject to processes or utilising materials that were promotional in nature and therefore inappropriate for a disease awareness team.

The CCDAT representatives' objectives and bonus criteria together with their training, briefing and health professional materials clearly demonstrated the non-promotional nature of this team.

The CCDAT team was primarily measured on activity based criteria with flexible objectives based on other criteria eg budget expenditure and planning which did not relate to promotional activity now or in the future. The bonus for the team from September to December 2006 would be based on an overall company performance (bonus level) and an individual 'multiplier' based on the team's performance against their non-promotional objectives.

The job specifications and advertisement used to recruit the team showed that at the launch of GlaxoSmithKline's candidate HPV vaccine, it was the company's intention that this team would most likely become a promotional team supporting the launch of the product. The objectives for the team would change at this point. GlaxoSmithKline was confident that it had taken great care and consideration to clearly separate these phases of activity in accordance with the spirit and the letter of the Code.

In its complaint, Sanofi Pasteur MSD alleged that 'it is impossible for the CCDAT's activities to be non-promotional for a number of reasons'. These reasons were addressed as follows:

- **'Potential prescribers are targeted through one-to-one contact, either in surgeries or at meetings'**

Primary care professionals who took the lead on, or who were involved in, cervical screening had been targeted in GlaxoSmithKline's disease awareness campaign because the education offered by the CCDAT would be of most relevance to them. The audience would be expected to consist of both prescribers and non-prescribers – not just 'potential prescribers' as stated by Sanofi Pasteur MSD. It was perfectly legitimate for non-promotional representatives to call directly on these health professionals to discuss disease awareness on a one-to-one basis or at educational meetings. Sanofi Pasteur MSD alleged that by engaging with health professionals in this way 'it is impossible for the team's activities to be non-promotional'. Sanofi Pasteur MSD had provided no evidence to substantiate this allegation other than some conjectural 'reasons'. GlaxoSmithKline strongly refuted this allegation and consequently a breach of Clause 3.1.

- **'Awareness of vaccines against cervical cancer is high amongst health professionals'**

GlaxoSmithKline was not aware of the data used to support this claim, although it was aware that knowledge amongst health professionals about the role of oncogenic HPV in cervical cancer was limited as previously referenced. The CCDAT was strictly non-promotional and disease focussed. It was acknowledged that there was some awareness of HPV vaccination among health professionals and, as such, this topic might be raised. As part of GlaxoSmithKline's risk management strategy to avoid

precisely the allegation that had been made, its non-promotional representatives had been thoroughly trained and assessed on how to handle potential situations from health professionals about HPV vaccination, specifically in order to prevent any discussion about unlicensed products. GlaxoSmithKline had gone to great lengths to ensure that the CCDAT responded to any such situation in a consistent and professional manner; thus the following statement was clearly outlined in the representatives' briefing document:

'GSK has a research and development interest in the area of cervical cancer. It is very common for manufacturers to provide medical education on relevant disease areas and the purpose of my visit today is to discuss CCa disease awareness, and not specific products.'

If a health professional was persistent in a request for information regarding HPV vaccination the CCDAT had been instructed to refer that health professional to the company's medical information department. The following statement had been included in the representatives' briefing document, which was only to be used reactively in response to persistent requests for information regarding specific products:

'The purpose of my visit today is to discuss CCa disease awareness, and not specific products. GSK's Medical Information Team will be able to assist you with any specific product enquiries.'

This was the process for enquiries relating to any unlicensed GlaxoSmithKline medicine or indication and was reiterated in Clause 2.2 of GlaxoSmithKline's own European Code of Practice which was in line with the ABPI Code. Contrary to Sanofi Pasteur MSD's assertion, the company's acknowledgement and proactive training on this topic was one of probity, not promotion, and took into account previous rulings. GlaxoSmithKline therefore strongly disagreed that this constituted a breach of Clause 3.1.

- **'GlaxoSmithKline is one of the largest vaccine suppliers in the UK'**

GlaxoSmithKline was the largest UK-based pharmaceutical company and manufactured medicines for a wide variety of therapy areas that might be known to primary care professionals. It disagreed with Sanofi Pasteur MSD's implication, by association rather than evidence, that GlaxoSmithKline's vaccine heritage meant that it was 'impossible for the team's activities to be non-promotional'.

- **'The activities of the team are bound to, and have, prompted questions about vaccination, and hence GlaxoSmithKline's candidate HPV vaccine'**

GlaxoSmithKline again stressed the safeguards that it had put in place to specifically prevent discussion about unlicensed products. All of its non-promotional representatives had a background in the pharmaceutical industry and a good working knowledge of the Code. They were fully aware of the important ethical regulations surrounding disease awareness activities. In addition, as already mentioned, they had been thoroughly trained and assessed on how to handle potential questions from health professionals about HPV vaccination, and were supported by their non-promotional area managers and the wider organisation to operate in accordance with the Code and the company's own high ethical standards. GlaxoSmithKline did not consider that the provision of genuine disease awareness education in this area amounted to soliciting questions on its HPV vaccination. The company denied a breach of Clause 3.1.

Sanofi Pasteur MSD then went on to state that the same representatives would be leading the launch of GlaxoSmithKline's candidate vaccine on their territory. This assertion had come directly from the recruitment advertisement, but Sanofi Pasteur MSD was confusing the fact that promotional activities had not and would not happen until such time as GlaxoSmithKline's candidate vaccine was approved and launched. Any subsequent promotion would be consistent with the marketing authorization for the vaccine. A decision upon the precise role of the staff in the CCDAT would be made based upon the best use of resources. Although Sanofi Pasteur MSD alleged a breach of Clause 3.1 because of the nature of the advertisement, it had incorrectly assumed that the CCDAT's activities were currently promotional. This was not the case. All current activities were strictly educational. No promotional activity was ongoing.

GlaxoSmithKline had stringent safeguards for the separation of non-promotional and promotional roles and although some of these CCDAT individuals might become promotional once the vaccine was approved, they were not conducting any promotional activity either directly or indirectly in their activities within the CCDAT. To allege a breach of Clause 3.1 based on a strategic plan when no promotion had taken place suggested that Sanofi Pasteur MSD had misunderstood the 'modus operandi' of the CCDAT.

Educational materials used by the CCDAT – leavepiece (CER/LVP/06/27063/1) and brochures (CER/DAP/06/26681/1)

Sanofi Pasteur MSD had cited examples of materials used by the CCDAT. It correctly stated that the materials followed a common theme (the objectives of the CCDAT were to raise awareness about the burden of cervical cancer, the causal role of oncogenic HPV in cervical cancer and the importance of regular screening). However, Sanofi Pasteur MSD raised concerns about some of the wording contained within these materials. It alleged that the combination of the mention of HPV types 16 and 18, reference to immunity and the fact that GlaxoSmithKline was one of the largest vaccine manufacturers in the UK made it highly likely that these materials would lead to questions about HPV vaccination and GlaxoSmithKline's candidate vaccine.

GlaxoSmithKline did not agree that the use of the word 'immunity' in the context of HPV types 16 and 18 would inevitably lead to questions about its candidate

vaccine. These specific types had been mentioned because they were the types responsible for around 70% of cervical cancer cases. An educational document about oncogenic HPV and its relationship to cervical cancer would not be complete without this information.

The immune system played a role in very many disease states, so the suggestion that the discussion of immunity would inevitably lead to questions about HPV vaccination was speculative and unfounded. The statement *'Previous infection with HPV may not provide sufficient immunity to prevent another infection'* was highly relevant in an educational document on the importance of regular cervical screening – it emphasised the need for continued regular screening in older women who remained sexually active, even if they had been treated for cervical lesions in the past, as they could never be considered 'immune' to oncogenic HPV infections.

All of the information contained within the materials was factual, balanced and fully referenced. It reflected key epidemiological and clinical data on cervical cancer and HPV. GlaxoSmithKline believed it essential to include all of this information in order to communicate a complete picture of the disease. All of this material had been through GlaxoSmithKline's approval process and had been certified as non-promotional.

Materials employed by the CCDAT – exhibition panels (CER/EXP/06/27062/1)

GlaxoSmithKline submitted that all of the information contained on the exhibition panels was factual, balanced and fully referenced. The panels always appeared together and, as such, highlighted the burden of disease, the causal role of oncogenic HPV and the importance of regular screening. At the bottom of each exhibition panel was the clear statement 'Regular cervical screening is vital in the fight against cervical cancer'. As above, these panels had also been approved as non-promotional material.

In conclusion, GlaxoSmithKline strongly refuted Sanofi Pasteur MSD's allegations and reiterated that it had taken the spirit and letter of the Code to heart in the recruitment of the CCDAT and in the planning and implementation of its activities. In summary:

- The highly trained non-promotional representatives' 'raison d'etre' was to increase awareness and understanding amongst relevant health professionals of the burden associated with cervical cancer, the causal role of oncogenic HPV and the importance of regular cervical screening.
- All of these non-promotional representatives (25% of whom came from a non-sales' background in GlaxoSmithKline) had been fully trained, assessed and were supported by their non-promotional area managers and the wider organisation to operate in accordance with the Code and the company's own ethical standards.
- GlaxoSmithKline's non-promotional representatives had not been trained on its HPV candidate vaccine as their discussions with health professionals were strictly disease focussed. The non-promotional nature of the CCDAT was also supported by objectives and bonus criteria for the team, briefing documents and training materials.
- All educational materials used by the CCDAT were educational and non-promotional in nature. The material was factual, balanced and fully referenced and reflected key epidemiological and clinical data on cervical cancer and HPV. It had not been designed to solicit questions on GlaxoSmithKline's candidate HPV vaccine.

GlaxoSmithKline considered that the ethos and activities of its CCDAT complied with the Code and denied that Clauses 3.1 and 2 had been breached.

PANEL RULING

The Panel noted that the Code permitted certain activities prior to the grant of the 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 providing that any such information or activity did not constitute promotion prohibited by Clause 3 or any other clause.

In the Panel's view the closer to the grant of the marketing authorization for a product the more difficult it was to argue that activities were a legitimate exchange of medical and scientific information during the development of a medicine.

The definition of promotion in Clause 1.2 did not include replies made in response to individual enquiries from members of the health professions or appropriate administrative staff or in response to specific communications from them whether of enquiry or comment, including letters published in professional journals, but only if they related solely to the subject matter of the letter or enquiry, were accurate and did not mislead and were not promotional in nature. The relevant supplementary information explained that this exemption applied to unsolicited enquiries only ie whereby companies responded to an enquiry having done nothing to prompt it. In answering an unsolicited enquiry a company could offer to provide further information. If the enquirer subsequently requested additional information this could be provided and would be exempt from the Code provided it met the requirements of the exemption. Information relating to human health or diseases was also exempt from the definition of promotion provided there was no reference either direct or indirect to specific medicines.

In the Panel's view it was not necessarily unacceptable for companies to have employees focussing on the provision of information prior to the grant of the marketing authorization. The arrangements and activities of such employees had to comply with the Code. Such employees should be comprehensively briefed about the Code. The area was difficult and companies needed to ensure that the arrangements and

activities were very carefully controlled and managed. The importance of documentation and instruction could not be overestimated.

The Panel noted GlaxoSmithKline's submission that the role of CCDAT was to educate relevant health professionals about the burden of cervical cancer and precancerous lesions, the causal role of oncogenic HPV in cervical cancer and the importance of the screening programme.

A detail aid (CER/DAP/06/26681/1) 'Cervical cancer - a major health issue for women' discussed the incidence and cause of cervical cancer and the success of cervical screening in the UK. A bullet point read 'Previous infection with HPV may not provide sufficient immunity to prevent another infection'. The brochure concluded with 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer' above 'Cervical cancer prevention for all women' in logo format. Identical statements appeared in a smaller, abridged leavepiece (20959476 CER/LVP/06/27063/1) which bore an identical title. Banner headlines on each of the three exhibition panels provided, discussed either the cause, incidence and/or burden of cervical cancer, one stating that '… previous infection with HPV may not provide sufficient immunity to prevent another infection'. Each concluded with the strapline 'Regular cervical screening is vital in the fight against cervical cancer'. A smaller exhibition panel (20959475 CER/EXP/06/27062/1) simply read 'Cervical cancer prevention for all women'. The GlaxoSmithKline logo appeared in the top left hand corner.

The representatives' briefing document, 'Cervical Cancer Disease Awareness Campaign', provided detailed information on the discussion points in the detail aid and leavepiece described above. The need to comply with the Code was highlighted. Representatives were told that '… it is possible that [health professionals] may ask about HPV vaccination and/or GlaxoSmithKline's vaccine in development, which **must not** be discussed under any circumstances'. A section headed 'To watch out for' gave three model answers. Firstly, to use if health professionals asked about why the representatives were talking about cervical cancer and not selling a product. Secondly, to use after Sanofi Pasteur MSD's product has been launched. If asked specifically about GlaxoSmithKline's candidate HPV vaccine representatives were advised to state that the purpose of the visit was to discuss cervical cancer disease awareness and not specific products and that GlaxoSmithKline's medical information team would be able to assist with any specific product enquiries. The representatives' disease awareness training material did not discuss medicines; it concluded with a section on screening and diagnosis.

The Panel considered that the material would encourage discussion about cervical cancer. This was not necessarily unacceptable so long as the material did not solicit questions about a specific medicine and that any discussion complied with the Code. The references to previous infection not providing sufficient immunity to prevent another infection might solicit general questions about vaccination. Whilst the Panel noted GlaxoSmithKline's explanation that such references emphasised the need for continued regular screening in older woman who remained sexually active the Panel did not consider that this explanation was made clear in any of the materials. Nonetheless, the overall emphasis of each item was on the burden and cause of disease and the need to ensure access to a successful screening programme. The Panel considered that the unqualified statement 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer' would encourage doctors to ask about GlaxoSmithKline's role in prevention. The Panel noted that the model answers provided in the representatives' briefing document all indicated that the representative should state that the purpose of their visit was to discuss cervical cancer disease awareness, and not specific products.

Overall the Panel considered that the material and activities of the representatives did not identify, directly or indirectly, a specific medicine such that GlaxoSmithKline's medicine was being promoted prior to the grant of its marketing authorization. Nor did the material solicit enquiries about GlaxoSmithKline's forthcoming product. No breach of Clause 3.1 was ruled. The Panel consequently ruled no breach of Clause 2.

APPEAL BY SANOFI PASTEUR MSD

Sanofi Pasteur MSD noted that GlaxoSmithKline had recruited a team of representatives and area managers whose current role was to promote disease awareness of cervical cancer - the CCDAT. The advertisement placed to recruit these individuals stated that, following the launch of GlaxoSmithKline's candidate HPV vaccine, the team would switch from promoting disease awareness to promoting the vaccine. Sanofi Pasteur MSD alleged that the existence and activities of the CCDAT were in breach of Clause 3.1 of the Code. The manner in which the team was recruited, the inexorably close ties between disease awareness and future brand success, and the materials and tactics employed inevitably promoted a product prior to receipt of its marketing authorization. Furthermore, this represented a new and worrying precedent in the activities of field-based representatives: disease awareness directed one to one at future prescribers pre-launch to be followed by traditional promotion post-launch. As well as breaching Clause 3.1 in the pre-launch phase, the prominence of the CCDAT, the inexorable link between disease awareness and future commercial promotional objectives, and the extent of its activities brought discredit upon, and reduced confidence in, the pharmaceutical industry as a whole and thus was in breach of Clause 2 of the Code.

Sanofi Pasteur MSD stated that GlaxoSmithKline had misunderstood, or chosen to misrepresent, its understanding of the recruitment advertisement for the CCDAT. Before the launch of its candidate vaccine representatives would be asked to raise awareness of cervical cancer; after the launch they would be asked to

promote the vaccine itself. This was evident from the advertisement. However, in its response, GlaxoSmithKline had stated that a decision upon the precise role of the CCDAT would be made based upon the best use of resources. This deviated from the advertisement where the two elements were inexorably linked.

Sanofi Pasteur MSD alleged that GlaxoSmithKline had argued that the CCDAT's objectives and bonus criteria indicated its non-promotional nature. Yet, in the longer term this team, primarily composed of sales professionals, hoped to be involved in the launch of its candidate vaccine. One therefore could not only consider the influence of short term objectives, but also needed to consider the longer term influence of future 'sales performance on your territory' (quoted from the advertisement).

Sanofi Pasteur MSD noted that GlaxoSmithKline had stated that the target audience of the CCDAT was primary care professionals who took the lead on, or who were involved in, cervical screening. It also stated that the objective of the CCDAT was to educate relevant health professionals about the burden of cervical cancer and precancerous lesions, the causal role of oncogenic HPV in cervical cancer and the importance of the screening programme. Sanofi Pasteur MSD alleged that these were somewhat at odds. Those involved in cervical screening, which had existed as an organised programme since 1988, were likely to be the best informed about the subject matter of the CCDAT, so why would they be the target audience for an educational programme?

Sanofi Pasteur MSD alleged that GlaxoSmithKline had acknowledged not only that its representatives might be asked why they were talking about cervical cancer and not selling a product, but also that they might be asked about HPV vaccination itself. The model answers attempted to deflect these questions but the answers would stimulate further enquiry. For example, the answer that GlaxoSmithKline had a research and development interest in cervical cancer was bound to result in further questioning about the nature of that interest. The final answer in the chain of escalation referred the health professional to GlaxoSmithKline's medical information team for 'specific product enquiries'. Since such questions could not be considered truly unsolicited, the responses provided, even if under the responsibility of the medical department, should be considered promotional. Sanofi Pasteur MSD queried if the Panel had requested information from GlaxoSmithKline about the number of enquiries its medical information team had answered that were stimulated by the CCDAT, and whether their content had been scrutinised.

Sanofi Pasteur MSD alleged that the level of enquiry from health professionals would be influenced by the level of public relations activity surrounding GlaxoSmithKline's candidate vaccine. For example, the following were recent press releases from GlaxoSmithKline's website (accessed 29 January 2007) that related to its candidate vaccine:

January 18 2007:	GlaxoSmithKline initiated head-to-head study of cervical cancer vaccines
September 29 2006:	Mathematical model predicted that Cervarix might prevent nearly 80% of cervical cancers
July 12 2006:	Latest data show GlaxoSmithKline's proprietary adjuvant system for Cervarix induced a stronger and more sustained immune response than a conventional adjuvant formulation

Sanofi Pasteur MSD noted that GlaxoSmithKline had refuted that its status as one of the largest vaccine suppliers in the UK had any bearing, referring to the fact that it manufactured medicines for a wide variety of therapeutic areas. GlaxoSmithKline had eighty eight prescription only brands listed in the Electronic Medicines Compendium. Sixteen of these were vaccines; six were in the field of oncology. The Panel had acknowledged that the materials employed by the CCDAT (a) would encourage doctors to ask about GlaxoSmithKline's role in cervical cancer prevention; and (b) might solicit general questions about vaccination. In this context, GlaxoSmithKline's prominence in the field of vaccines and relative lack of prominence in the field of oncology was important.

Sanofi Pasteur MSD alleged that finally, the focus on the oncogenic HPV types 16 and 18 (the two types targeted by GlaxoSmithKline's candidate vaccine) in the CCDAT materials, combined with the points described above, made it inevitable that the materials and activities of the CCDAT would solicit enquiries about GlaxoSmithKline's candidate vaccine. Indeed, this was acknowledged by GlaxoSmithKline itself in the questions and answers provided to its representatives.

Sanofi Pasteur MSD alleged that the material and the activities of the CCDAT had (a) indirectly identified GlaxoSmithKline's candidate HPV vaccine; and (b) solicited enquiries about it. Therefore Sanofi Pasteur MSD appealed the Panel's ruling of no breach of Clauses 3.1 and 2 of the Code.

With regard to GlaxoSmithKline's documents headed 'Performance and Development Plan' and 'Welcome to the Performance and Development planning process' Sanofi Pasteur MSD submitted that it had a number of concerns regarding the true motives for the CCDAT. GlaxoSmithKline had stated in its response that the CCDAT team was primarily measured on activity based criteria with flexible objectives based on other criteria eg budget expenditure and planning which did not relate to promotional activity now or in the future. Furthermore, GlaxoSmithKline also stated that it had stringent safeguards for the separation of non-promotional and promotional roles and that members of the CCDAT were not conducting any promotional activity either directly or indirectly.

Sanofi Pasteur MSD alleged that these two claims were at odds with some of the elements of the Performance and Development Plan for the area manager. The area

manager's department was referred to as 'CBU'; this stood for Cervarix business unit. That in itself spoke volumes. The fact that the area managers were an integral part of a business unit whose remit must be to deliver commercial success for Cervarix showed flagrant disregard for the spirit and the letter of the Code.

Additionally, Sanofi Pasteur MSD noted the following objectives were of specific concern.

The final performance measure listed was '2-way communication with brand team'. If non-promotional and promotional roles were so stringently separated, why would the CCDAT area managers need to communicate with the brand team?

Although the section on specific alignments was not completed, it was totally inappropriate to even refer to 'achieving expectations for brand champions' in the performance and development plan for an allegedly non-promotional role.

The endorsement section appeared to refer to endorsement from 'customers' at regional and national level. A number of issues caused concern:

(a) The reference to 'customers', a term that was traditionally used in a commercial context.
(b) 'Role clarity in terms of ownership and responsibilities agreed with [named manager]'. This presumably referred to who would be responsible for each 'customer'. That manager was the Senior Brand Manager, Vaccines, for GlaxoSmithKline. This was further evidence of the intertwined relationship between the allegedly non-promotional CCDAT and the brand team.
(c) 'KOL [key opinion leader] mobilisation plan in place'. Typically key opinion leader referred to respected, knowledgeable and influential health professionals. It would be instructive to know what they were being mobilised to do and why the plan was only to be put in place, rather than executed. Perhaps the execution was for a later time.

Sanofi Pasteur MSD alleged in summary that the content of the area manager's performance and development plan reinforced its concerns about the existence and activities of the CCDAT.

COMMENTS FROM GLAXOSMITHKLINE

GlaxoSmithKline assured the Appeal Board that it had taken the spirit and letter of the Code to heart in the recruitment of the CCDAT and in the planning and implementation of its activities. As such, GlaxoSmithKline was confident that the existence of this non-promotional team and its activities complied with the Code. GlaxoSmithKline supported the Panel in its interpretation and ruling on the comprehensive response submitted to the original complaint.

GlaxoSmithKline submitted that it appeared that Sanofi Pasteur MSD's appeal was anchored to the content of the initial recruitment advertisement. The content and intent of the advertisement alluded to the team changing its objectives once a marketing authorization was granted for the company's candidate HPV vaccine. However, the CCDAT was an entirely non-promotional team which was engaged in a genuine disease awareness campaign. The non-promotional nature of the team was evidenced by the CCDAT briefing document, training, health professional materials and objectives and bonus criteria together with the comprehensive material and guidance on handling possible questions from health professionals.

GlaxoSmithKline submitted that in future, individuals from the CCDAT might become part of a promotional team which would support the product when it was licensed. The training, materials, objectives and bonus criteria for any such new team would reflect its promotional nature and as such, would be completely different from those of the non-promotional CCDAT. The existence and activities of the CCDAT could only be judged by what was happening now, not what activities might or might not be undertaken by a promotional team in the future. The CCDAT did not discuss HPV vaccination under any circumstances and had been thoroughly trained and assessed on how to handle potential situations where health professionals might ask about HPV vaccination. Contrary to Sanofi Pasteur MSD's assertion, the company's proactive approach and training on this topic was one of probity, not promotion, and took into account previous rulings.

GlaxoSmithKline addressed Sanofi Pasteur MSD's assertion that those involved in cervical screening, which had existed as an organised programme since 1988, were likely to be the best informed about the subject matter of the CCDAT. This statement was addressed by the publications cited previously which highlighted the need for further education of health professionals in this area, a conclusion which was also supported by market research commissioned by GlaxoSmithKline. GPs and most practice nurses were involved in cervical screening as they provided the backbone of the national cervical screening programme. GlaxoSmithKline decided to target those health professionals who had shown an active interest in cervical cancer as the information was likely to be of more interest and relevance to them. They were also more likely to be concerned about the dramatic decline in uptake of screening in younger women and be keen to motivate all of their eligible female patients to attend. Raising health professionals awareness in this area in a way that might subsequently improve patient care could only be a positive outcome.

In response to Sanofi Pasteur MSD's allegation regarding the public relations activity undertaken by GlaxoSmithKline, all three press releases clearly related to important events in the vaccine development programme and did not constitute a concerted public relations campaign to drive enquiries from health professionals as inferred.

GlaxoSmithKline noted that Sanofi Pasteur MSD had alleged that its prominence in the field of vaccines and relative lack of prominence in oncology was important.

GlaxoSmithKline was the largest UK-based pharmaceutical company and manufactured medicines for a wide variety of therapy areas that might be known to primary care health professionals. Health professionals did not make an inevitable assumption that it was developing a vaccine for cervical cancer as no specific medicine was referred to, either directly or indirectly, in any of the CCDAT materials or activities.

GlaxoSmithKline noted that Sanofi Pasteur MSD re-iterated its claim that there was a focus on oncogenic HPV types 16 and 18 and that this invited enquiries about GlaxoSmithKline's candidate vaccine, as these two HPV types were targeted by its vaccine. As previously outlined, the material made it clear that there were around 100 types of HPV, of which 15 could cause cervical cancer but types 16 and 18 were responsible for the majority, representing over 70% of cases.

In summary, GlaxoSmithKline submitted that the CCDAT was non-promotional; educated doctors and nurses on the epidemiology, burden and prevention of cervical cancer through screening. None of the materials or activities either directly or indirectly referred to specific medicines or encouraged enquiries about unlicensed products. The team had been thoroughly briefed on the Code and how to work within it. It had not been trained on any products in this therapeutic area, and had been instructed to refer any queries about medicines to medical information. GlaxoSmithKline had taken a responsible approach to training the representatives to ensure they operated within the Code and were aware of potential pitfalls.

GlaxoSmithKline noted Sanofi Pasteur MSD's additional comments on its 'Performance and Development Plan' and 'Performance and Development Plan Planning Process' documents.

GlaxoSmithKline re-iterated that the CCDAT was not measured or incentivised on criteria that would encourage the representatives to promote its candidate HPV vaccine, Cervarix, prior to it receiving its marketing authorization and this was quite clear from the 'Performance and Development Plan'. Sanofi Pasteur MSD's latest concerns appeared to centre around its assumptions based on terminology and nomenclature.

GlaxoSmithKline submitted that the department within the company responsible for the CCDAT was correctly identified as the Cervarix business unit (CBU). This title was strictly not referred to in interactions with health professionals. As such, it did not appear on business cards and was not referenced in any verbal or written correspondence with health professionals. GlaxoSmithKline was comprised of a number of business units which were each responsible for all activities related to its major brands and the associated disease areas. The CCDAT activities, materials, training, objectives and bonus criteria clearly established the CCDAT as a non-promotional team and the fact that they were part of the Cervarix business unit **did not** influence the nature of their role. Both product and non-product related activities fell within the remit of the Ceravix business unit and all members of the UK company who worked on GlaxoSmithKline's candidate HPV vaccine formed part of the Cervarix business unit.

GlaxoSmithKline submitted that all CCDAT activities, materials, guidance and training were certified to ensure compliance with both the spirit and letter of the Code. The CCDAT undertook no promotional activity as evidenced by the information provided to and ruled on by the Panel. GlaxoSmithKline strongly refuted Sanofi Pasteur MSD's allegation of 'flagrant disregard' for the Code.

GlaxoSmithKline submitted that as evidenced by previous correspondence on this case, disease awareness activities were permitted under the Code and in the Medicines and Healthcare products Regulatory Agency's (MHRA) Blue Guide S5.11 as quoted below.

'Campaigns relating to human health directed at the general public with a view to providing information, promoting awareness or educating the public about a particular condition or disease are encouraged. Care must be taken to ensure that the information provided does not make product claims for the material to remain outside the definition of an "advertisement" under the Regulations. In particular, use of brand names, restricting the range of treatments described in the campaign or drawing attention to the campaign by advertising which is likely to lead to the use of a specific prescription only medicine or medicines can all lead to a potential breach of the Regulations.'

GlaxoSmithKline submitted that neither the Code nor the MHRA required disease awareness teams to have a specific reporting line. It was clear in all documentation that the requirements and the spirit of the Code and the MHRA Blue Guide had been strongly upheld by GlaxoSmithKline. It was customary practice in GlaxoSmithKline for non-promotional roles to be aligned with brand teams, and it was a source of pride that GlaxoSmithKline was able to achieve a clear distinction of promotional and non-promotional activities through its significant internal investment in its ongoing ethics programme.

GlaxoSmithKline submitted that with regard to the '2 way communication' with the brand team it was worth clarifying the constitution of a brand team. Within GlaxoSmithKline, the 'brand team' were not exclusively marketeers or sales people - medical advisors, researchers and scientific advisors also formed part of the team. The 'brand' referred to in the performance and development plan was cervical cancer disease awareness. As highlighted previously, the CCDAT team was exclusively focussed on cervical cancer disease awareness. As mentioned above, there was no restriction on the reporting line of disease awareness teams as long as the required separation occurred between product and non-product related activities. The CCDAT activities were purely non-promotional and non-product related.

GlaxoSmithKline submitted that none of the documentation referred to vaccination or any product

related to cervical cancer. GlaxoSmithKline reiterated the entirely non-promotional nature of the CCDAT and noted that Sanofi Pasteur MSD had not provided any evidence of any promotional activities being conducted by the CCDAT. This was because none existed.

GlaxoSmithKline submitted that in addition to the 'brand team' reference, Sanofi Pasteur MSD also highlighted additional areas of concern, particularly around the use of 'customers' and 'KOL [key opinion leader] mobilisation'. 'Customers' was an umbrella term used to identify the recipient of goods or a service. However, its use was not restricted to a commercial context within GlaxoSmithKline, where, for example, medical information teams also referred to health professionals as their 'customers'. In the context of the CCDAT, 'customer' referred to the recipient of the cervical cancer disease awareness educational programme. 'Endorsement' from customers at a regional and national level referred to health professional agreement with and support of the need for education in the area of cervical cancer. The level of their endorsement might vary from simply agreeing with the need for further education in this area, to being prepared to speak locally or nationally about cervical cancer, and one of the aims of the CCDAT was to mobilise key opinion leaders to educate other health professionals about this disease area. As with all CCDAT activities, the content of such educational sessions was entirely disease focussed.

With regard to Sanofi Pasteur MSD's allegation about one of its managers, GlaxoSmithKline explained that he was a senior brand manager within the Cervarix business unit. His role was focussed on external health professionals relationships and meeting arrangements and he oversaw the planning and logistics of external meetings within the Cervarix business unit. As such, it was entirely appropriate that he and the CCDAT would communicate with each other regarding the educational meetings outlined above, and this was entirely in line with their non-promotional role. The bullet point in the performance and development plan referred to CCDAT clarity in terms of key opinion leader contact. The CCDAT consisted of 65 educational representatives. Therefore, in order to limit the frequency and volume of requests made of each key opinion leader, each key opinion leader had one point of contact within GlaxoSmithKline. The management of this process fell within the manager's remit.

GlaxoSmithKline submitted that in summary, none of the area managers' performance and development plans referred directly or indirectly to either increasing health professional's knowledge, or sales, of GlaxoSmithKline's candidate HPV vaccine. Furthermore, none of the CCDAT's materials or activities referred to specific medicines either directly or indirectly, nor did they encourage enquiries about unlicensed products. The CCDAT had not been trained on HPV vaccination and did not discuss HPV vaccination with health professionals under any circumstances. In addition, they had been rigorously trained on how to deal with situations in which the health professionals raised the subject of HPV vaccination.

GlaxoSmithKline submitted that it had clearly not promoted any medicine in advance of its marketing authorization. As such it urged the Appeal Board to uphold the Panel's ruling of no breach of Clause 3.1 and thus Clause 2.

FURTHER COMMENTS FROM SANOFI PASTEUR MSD

Sanofi Pasteur MSD noted that GlaxoSmithKline had stated that no evidence existed of any promotional activities having been conducted by the CCDAT. However, Sanofi Pasteur MSD alleged that it had feedback from its own representatives both of CCDAT representatives actively mentioning vaccination and also of customers asking CCDAT representatives about vaccination. These were not isolated incidents and no doubt reflected (a) the inherent difficulties in constructing a disease awareness team that would have future promotional responsibilities; and (b) the difficulty in a pharmaceutical company field-based team conducting disease awareness with no product mention and the inevitable questions that would be raised by health professionals.

APPEAL BOARD RULING

In the Appeal Board's view it was not necessarily unacceptable for companies to conduct a disease awareness campaign and to use materials with health professionals that generated discussion prior to the grant of a relevant marketing authorization. The arrangements had to comply with the Code. Employees involved in delivering such a campaign should be comprehensively briefed about the Code. The area was difficult and companies needed to ensure that the arrangements and activities were very carefully controlled and managed. The importance of documentation and instruction could not be overestimated. All of the circumstances had to be taken into account when deciding whether such arrangements complied with the Code.

The Appeal Board noted that the recruitment advertisement that appeared in the April 2006 issue of Pharmaceutical Field, a journal aimed at sales professionals, stipulated that candidates for the position of representatives should have a proven track record in sales, with excellent negotiation and influencing skills. The advertisement referred to delivering a focussed disease awareness campaign and then implementing the launch of the vaccine in early 2007. The Appeal Board considered that whilst a sales background was not necessarily unacceptable it was however, consequently important that the company was especially careful about the arrangements and activities given a representative's natural tendency to sell. The Appeal Board also noted the company representatives' submission that approximately 25% of the CCDAT team was recruited from a non-sales position.

The Appeal Board noted GlaxoSmithKline's submission about the CCDAT non promotional role

and training but was nonetheless concerned about the scale of the activity; there were 65 members of the CCDAT operating throughout the UK, targeting potential prescribers. It was likely that most of the CCDAT would promote GlaxoSmithKline's vaccine to the same group of prescribers once the product had received its marketing authorization.

The Appeal Board did not accept the GlaxoSmithKline representatives' position that the primary purpose of the CCDAT and materials was to increase screening rates. The company representatives had explained that the targeted practices were those with large numbers of female patients registered and not those with low uptake of cervical screening.

The Appeal Board noted that HPV types 16 and 18 were responsible for 71.5% of cervical cancers. Fifteen of the 100 HPV types identified could cause cervical cancer. The Appeal Board was concerned about the overall emphasis of the detail aid (CER/DAP/06/26681/1) on HPV types, particularly oncogenic HPV types 16 and 18, given the stated primary objective of the campaign to increase screening levels. The Appeal Board considered that this objective could be achieved without such emphasis. In particular three out of four bullet points on the final page of text (page 13), which the Appeal Board inferred summarized the key take-home message of the detail aid, referred to oncogenic HPV types 16 and 18 and/ or HPV infection. There was no mention of screening. Further the references to and undue emphasis on only oncogenic HPV types 16 and 18 could only relate to a specific medicine; GlaxoSmithKline's forthcoming vaccine. (The currently available vaccine Gardasil, was indicated for HPV types 6 and 11 as well as oncogenic HPV types 16 and 18.) The page also stated that 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer'. The company representatives explained that the support referred to comprised discussion with health professionals by members of the CCDAT about the importance of screening, sponsorship of educational meetings and the provision of patient leaflets. The Appeal Board did not have copies of the patient leaflets before it.

Overall the Appeal Board considered that the cumulative effect of the arrangements amounted to promotion of a product prior to the grant of its marketing authorization. A breach of Clause 3.1 of the Code was ruled. It thus considered that the arrangements would bring discredit upon and reduce confidence in the pharmaceutical industry; a breach of Clause 2 was ruled. The appeal was successful.

Complaint received **3 November 2006**

Case completed **2 May 2007**

ROCHE and GLAXOSMITHKLINE v PROCTER & GAMBLE and SANOFI-AVENTIS

Disparagement of Bonviva

Roche complained on behalf of itself and GlaxoSmithKline about a slide kit produced by Procter & Gamble and Sanofi-Aventis, acting as the Alliance for Better Bone Health. The slide kit presented data on Roche's product, Bonviva (ibandronate). Procter & Gamble and Sanofi-Aventis jointly promoted Actonel (risedronate).

Roche drew attention to supplementary evidence to support a previous complaint made by it and GlaxoSmithKline (Cases AUTH/1885/8/06 and AUTH/1886/8/06) in respect of activities undertaken by Procter & Gamble and Sanofi-Aventis which misled clinicians about the licensed indication for Bonviva and disparaged it and the existing evidence base.

The slide kit entitled 'Do all bisphosphonates have the same fracture efficacy? Non-vertebral Fracture Risk in Ibandronate Clinical Trials' was being proactively used as a promotional item and distributed to clinicians by Procter & Gamble and Sanofi-Aventis for use at speaker meetings. Its content was formed from the same data set used in the claim that ibandronate increased non-vertebral fracture in a subset of patients made at a Procter & Gamble and Sanofi-Aventis sponsored symposium in June 2006 and considered in Cases AUTH/1885/8/06 and AUTH/1886/8/06.

Roche and GlaxoSmithKline believed that because the slide kit was prepared in May, ie before the symposium in June, it contradicted the companies' contention in Cases AUTH/1885/8/06 and AUTH/1886/8/06 that the data presented was unknown to them and represented the speaker's opinion alone.

Roche alleged that the content of the slide kit was disparaging and was taken out of context from materials supplied to the Food and Drug Administration (FDA) as part of the original licence submission and thus breached the Code. This slide set and the slide used at the symposium purported to reflect analyses carried out by or endorsed by the FDA. In fact the link to the FDA website led only to a summary prepared by the FDA reviewers of clinical data submitted by Roche for licence approval in the US. This summary included a short section which examined a subgroup of patients in one of the pivotal studies who were at high risk of non-vertebral fracture and in which treatment with ibandronate led to a 69% decrease in fracture rate. An FDA annotation in this summary noted that the information was of academic interest but would not be included in the package insert. Procter & Gamble and Sanofi-Aventis however had included this analysis plus tables and other data in the clinical summary to construct a slide set designed to disparage Bonviva. Thus one of the slides was a construct which showed a higher fracture rate in patients with T score < -3 which was similar to the bar chart shown at the company sponsored symposium. The FDA reviewers did not perform this analysis although the slides misled the viewer to believe that they had. Indeed the juxtaposition of genuine FDA slide copies with slides constructed by Procter & Gamble and Sanofi-Aventis further misled as to the origin of the analysis especially as all the slides were referenced to the website. The way in which Procter & Gamble and Sanofi-Aventis were proactively distributing these data undermined confidence in the pharmaceutical industry in breach of Clause 2.

The Panel noted that the previous cases, Cases AUTH/1885/8/06 and AUTH/1886/8/06 concerned a slide headed 'Beware subgroup analyses!' used by an independent speaker at a symposium organized by Procter & Gamble and Sanofi-Aventis. The slide featured two bar charts: the first showed that in patients with a femoral neck bone mineral density (BMD) > -3.0, ibandronate increased fracture risk by 44% compared with placebo. The second bar chart showed a 64% decreased fracture risk compared with placebo in patients with a femoral neck BMD of < -3.0.

The slide was used to illustrate the dangers of sub-group analysis and featured clinical results about a product which was a direct competitor to that of the sponsor company. The Panel queried why other data could not have been used to illustrate the point. The Panel understood that the results shown, if true, might have been such as to prevent Bonviva obtaining a marketing authorization for the treatment of osteoporosis at least in a subgroup of patients. The Panel acknowledged the very limited use of the data and the context in which the slide was shown but nonetheless considered that Bonviva had been disparaged as alleged. A breach of the Code had been ruled.

Turning to the present complaint, Cases AUTH/1911/11/06 and AUTH/1912/11/06, the Panel noted that the slide kit at issue, entitled 'Do all bisphosphonates have the same fracture efficacy? Non-vertebral Fracture Risk in Ibandronate Clinical Trials', similarly presented analysis based on data from the FDA website. The material was, however, different to that considered in Cases AUTH/1885/8/06 and AUTH/1886/8/06. The Panel noted that there was no allegation of a breach of undertaking and that the slide kit had, in any event, been withdrawn pursuant to the earlier cases.

Slide 14 of the set featured a table headed 'Non-vertebral fractures in women with femoral neck T-score above and below -3.0 SD' which was 'Deduced from

tables presented on pages 25 and 26 of the FDA report'. The number of non-vertebral osteoporotic fractures for the ITT population subjects with femoral neck T-score above -3SD was 47 for placebo and 68 for Bonviva 2.5mg. This data was reproduced in graphs on two subsequent slides, one of which showed that patients with a baseline femoral neck BMD T-score ≥ - 3 SD represented 87% of the patient population (ITT). The Panel also noted that some slides featured tables headed 'FDA Medical Review of Ibandronate' and cited the relevant report page. Some slides featured graphs which were not similarly headed but featured the relevant FDA website address in the bottom right-hand corner. Two tables explained data was 'deduced' from tables in the FDA report. Other slides did not refer to the FDA.

The Panel considered that the data showing increased fracture risk disparaged Bonviva as alleged. A breach of the Code was ruled. Further, the Panel considered that juxtaposing FDA data with material created by Procter & Gamble and Sanofi-Aventis, and slides which gave no indication of the material's origin were such that the origin of the analyses was not sufficiently clear. Readers might gain the impression that data regarding the increased fracture risk in patients with a baseline femoral neck BMD T-score ≥ - 3 SD was consistent with the relevant FDA report which was not so. The material was misleading in this regard. A breach of the Code was ruled.

The Panel did not consider that use of material was in breach of Clause 2 of the Code which was used as a sign of particular censure and reserved for such use.

Roche Products Limited complained on behalf of itself and GlaxoSmithKline UK Ltd about a slide kit (ACT 3206) produced by Procter & Gamble Pharmaceuticals UK Ltd and Sanofi-Aventis, acting as the Alliance for Better Bone Health. The slide kit presented data on Roche's product, Bonviva (ibandronate). Procter & Gamble and Sanofi-Aventis jointly promoted Actonel (risedronate).

COMPLAINT

Roche drew attention to supplementary evidence to support the complaint made by it and GlaxoSmithKline (Cases AUTH/1885/8/06 and AUTH/1886/8/06) in respect of activities undertaken by Procter & Gamble and Sanofi-Aventis which misled clinicians about the licensed indication for Bonviva and disparaged it and the existing evidence base.

The slide kit entitled 'Do all bisphosphonates have the same fracture efficacy? Non-vertebral Fracture Risk in Ibandronate Clinical Trials' was being proactively used and distributed as a promotional item by Procter & Gamble and Sanofi-Aventis. Its content was formed from the same data set used in the claim that ibandronate increased non-vertebral fracture in a subset of patients made at the symposium sponsored by Procter & Gamble and Sanofi-Aventis at the National Osteoporosis Society meeting held in Harrogate (25-28 June). This was originally considered in Cases AUTH/1885/8/06 and AUTH/1886/8/06.

Roche and GlaxoSmithKline believed that because the preparation date of the slide kit (May 2006) preceded the symposium (June 2006) it contradicted the companies' contention in Cases AUTH/1885/8/06 and AUTH/1886/8/06 that the data presented was unknown to them and represented the speaker's opinion alone.

Roche also alleged that the slide kit was being actively used as a promotional item and proactively distributed to clinicians for use at speaker meetings. The content was clearly disparaging and was taken out of context from materials supplied to the Food and Drug Administration (FDA) as part of the original licence submission and thus breached Clauses 8.1 and 7.2 of the Code. This slide set and the slide used at the symposium were used as if they reflected analyses carried out by or endorsed by the FDA. In fact the link to the FDA website led only to a summary prepared by the FDA reviewers of clinical data submitted by Roche for licence approval in the US. Included in this summary of clinical data was a short section which examined a subgroup of patients in one of the pivotal studies who were at high risk of non-vertebral fracture and in which treatment with ibandronate led to a 69% decrease in fracture rate. An FDA annotation in this summary noted that the information was of academic interest but would not be included in the package insert. Procter & Gamble and Sanofi-Aventis however had included this analysis plus tables and other data in the clinical summary to construct a slide set designed to disparage the evidence base for effectiveness of Bonviva at non-vertebral sites and to disparage Bonviva effectiveness in general. Thus one of the slides was a construct which showed a higher fracture rate in patients with T score < -3 which was similar to the bar chart shown at the company sponsored symposium. The FDA reviewers did not perform this analysis although the slides misled the viewer to believe that they had. Indeed the juxtaposition of genuine FDA slide copies with slides constructed by Procter & Gamble and Sanofi-Aventis further misled as to the origin of the analysis especially as all the slides were referenced in the same manner to the website. The manner in which Procter & Gamble and Sanofi-Aventis was proactively distributing these data undermined confidence in the pharmaceutical industry in breach of Clause 2.

Whilst the original complaint relating to the inappropriate statistical analysis did not claim that Procter & Gamble and Sanofi-Aventis' activities breached Clause 2, Roche and GlaxoSmithKline now believed that the activities had reduced confidence in the pharmaceutical industry. This was based on the concerted campaign to disparage Bonviva in combination with the abuse of Paragraph 5.2 of the Constitution and Procedure evidenced by the complete denial that they neither knew of the data presented at the symposium referred to in the original complaint or its active promotion via a slide kit thereafter despite direct questioning.

RESPONSE

Procter & Gamble and Sanofi-Aventis explained that the

slide kit in question 'Do all bisphosphonates have the same fracture efficacy?' was designed to provide scientific information on the non-vertebral fracture efficacy of Bonviva to thought leaders in osteoporosis. The 16 slides captured the evidence base on the ibandronate non-vertebral fracture efficacy. All efforts were taken to include all the data available in the public domain regarding the non-vertebral fracture efficacy of ibandronate. That was without making interpretations, performing analysis and omitting relevant fracture data.

Chesnut et al (2004), and study MF4411 (which was shared in the Medical Review of the FDA report and currently mentioned in section 5.1 of the Bonviva summary of product characteristics (SPC)) were shared accurately and were fairly represented. The allegations that the data had been altered, or misrepresented were untrue. Furthermore the data provided was sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine. If any more information was available the companies would welcome this input from Roche and GlaxoSmithKline. The companies denied breaches of Clauses 8.1 and 7.2.

The slides faithfully led the reader through the data starting with Chesnut *et al*, and clearly stated that there was no significant difference for the non-vertebral fracture levels between the placebo and active arms of the study. When depicting study MF4411 the slides clearly showed where the data was presented in the FDA website, and clearly stated that data was deduced. It was not claimed that ibandronate increased non-vertebral fracture in a subset of patients, nor was it implied that any analysis was performed by the FDA. The companies stressed that it would never intentionally bring discredit upon, or reduce confidence in, the pharmaceutical industry, and thus refuted any breach of Clause 2.

The companies noted that this data led to the Bonviva SPC revisions (Section 5.1) and was not only of academic interest as previously dismissed by Roche.

The companies acknowledged the ruling in Cases AUTH/1885/8/06 and AUTH/1886/8/06 and had withdrawn the slide kit.

PANEL RULING

The Panel noted that the previous cases, Cases AUTH/1885/8/06 and AUTH/1886/8/06 concerned a slide headed 'Beware subgroup analyses!' used by an independent speaker at a symposium organized by Procter & Gamble and Sanofi-Aventis. The slide featured two bar charts: the first showed that in patients with a femoral neck bone mineral density (BMD) > -3.0, ibandronate increased fracture risk by 44% compared with placebo. The second bar chart showed a 64% decreased fracture risk compared with placebo in patients with a femoral neck BMD of < -3.0.

The Panel noted that the slide was shown to delegates at a company-sponsored symposium and used to illustrate the dangers of sub-group analysis. The slide featured clinical results about a product which was a direct competitor to that of the sponsor company. The Panel queried why other data could not have been used to illustrate the point. The Panel understood that the results shown, if true, might have been such as to prevent Bonviva obtaining a marketing authorization for the treatment of osteoporosis at least in a subgroup of patients. The Panel acknowledged the very limited use of the data and the context in which the slide was shown but nonetheless considered that Bonviva had been disparaged as alleged. A breach of Clause 8.1 had been ruled.

Turning to the present complaint, Cases AUTH/1911/11/06 and AUTH/1912/11/06, the Panel noted that the slide kit at issue, entitled 'Do all bisphosphonates have the same fracture efficacy? Non-vertebral Fracture Risk in Ibandronate Clinical Trials', similarly presented analysis based on data from the FDA website. The material was, however, different to that considered in Cases AUTH/1885/8/06 and AUTH/1886/8/06. The Panel noted that there was no allegation of a breach of undertaking and that the slide kit had, in any event, been withdrawn pursuant to the earlier cases.

The Panel noted that slide 14 of the set featured a table headed 'Non-vertebral fractures in women with femoral neck T-score above and below -3.0 SD' which was 'Deduced from tables presented on pages 25 and 26 of the FDA report'. The number of non-vertebral osteoporotic fractures for the ITT population subjects with femoral neck T-score above -3SD was 47 for placebo and 68 for Bonviva 2.5mg. This data was reproduced in two subsequent graphs on slides 15 and 16, one of which showed that patients with a baseline femoral neck BMD T-score ≥ - 3 SD represented 87% of the patient population (ITT). The Panel also noted that some slides featured tables headed 'FDA Medical Review of Ibandronate' and cited the relevant report page. Some slides featured graphs which were not similarly headed but featured the relevant FDA website address in the bottom right-hand corner. Two tables explained data was 'deduced' from tables in the FDA report. Other slides did not refer to the FDA.

The Panel considered that the data showing increased fracture risk disparaged Bonviva as alleged. A breach of Clause 8.1 was ruled. Further, the Panel considered that the juxtaposing of FDA data with material created by Procter & Gamble and Sanofi-Aventis, and slides which gave no indication of the material's origin were such that the origin of the analyses was not sufficiently clear. Readers might gain the impression that data regarding the increased fracture risk in patients with a baseline femoral neck BMD T-score ≥ - 3 SD was consistent with the relevant FDA report which was not so. The material was misleading in this regard. A breach of Clause 7.2 was ruled.

The Panel did not consider that use of material was in breach of Clause 2 of the Code which was used as a sign of particular censure and reserved for such use.

Complaint received 7 November 2006

Case completed 5 March 2007

CASE AUTH/1913/11/06

DOCTOR v ASTELLAS PHARMA

Representative call rates

A doctor queried whether Astellas Pharma was in breach of the Code by asking its representatives to see dermatology consultants four times between mid October and Christmas. The complainant considered such conduct was close to harassment.

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

The briefing document, given to representatives in October 2006, stated 'Your objective is to see your Senior Grade Dermatologists 4 times by December 31 2006'. There was no explanation that, as submitted by Astellas, this was meant to be the number of contacts for the whole year, not just the period October to December. The Panel considered that without further explanation the briefing document advocated a course of action which was likely to breach the Code. A breach of the Code was ruled.

The Panel took the complaint as evidence that overcalling had actually occurred and in that regard noted that the complainant had referred to harassment. A further breach was ruled.

COMPLAINT

A doctor queried whether Astellas Pharma Ltd was in breach of the Code by asking its representatives to see dermatology consultants four times between mid October and Christmas. The complainant considered such conduct was close to harassment.

The Authority asked Astellas to bear in mind the requirements of Clauses 2, 15.4 and 15.9 of the Code.

RESPONSE

Astellas explained that a Skinsense Briefing Document was given to representatives with hospital responsibility attending a company sales conference held in October 2006. The representatives were responsible for seeing hospital doctors in urology as well as doctors specialising in dermatology. During the earlier part of 2006 the focus had been on urology and now the representatives were being asked to change this emphasis and ensure that they provided sufficient information to dermatology contacts particularly with regard to Protopic (tacrolimus).

In 2006 Protopic (together with the other topical calcineurin inhibitor) had been reviewed by both the European Medicines Evaluation Agency (EMEA) and the Food and Drug Administration (FDA) regarding a potential safety issue. The conclusion was that the risk:benefit ratio for Protopic remained unchanged. In particular there was no evidence of a link between the use of Protopic and certain skin cancers or lymphomas although the possibility of a link could not be completely excluded at this stage. The theoretical possibility of such a link had been postulated based on rates of malignancy in transplant patients receiving immunosuppressive agents including the systemic form of tacrolimus. Whilst the reviews were in progress, Astellas representatives had visited their dermatology contacts less often than would otherwise have been planned.

Following the publication of the reviews it was important that representatives had sufficient opportunities to discuss these complex issues with potential prescribers. Indeed several consultants had asked to see more of the Astellas sales team to discuss these issues. The launch of the Skinsense programme was an opportunity to include this type of discussion.

The representatives' briefing at the conference referred to all senior grade dermatologists of staff grade and above, including consultants and associate specialists. The briefing did not specify just consultant dermatologists. It was suggested that all senior grade dermatologists should be seen *in total* 4 times by 31 December 2006. This was an expectation for the whole year and to include all types of contacts rather than just direct calls. However Astellas accepted that this could have been made clearer in the briefing document as required by Clause 15.9 of the Code.

On reviewing call rates for 2006 thus far the average contact rate was 1.31. In 2005, Astellas had contacted senior dermatologists on average 0.73 times in the year.

Astellas expected senior grade dermatologists to be seen a total of up to 4 times by the end of the year because the company anticipated the likelihood of an additional call being requested to allow for questions and discussions in relation to the EMEA review. This represented total contacts and not just one-to-one visits. Representatives were therefore required to allow for this possible rate of contacts. The actual number of contacts would depend on the number already made up until that time. There was never any suggestion of doctors being subjected to 'harassment' and

representatives knew that the intervals between calls should also be appropriate. All calls would be made by appointment via departmental secretaries and any refusals would be respected.

Astellas had not received any negative response to the requests for appointments from any dermatologist. Indeed as mentioned above, the opportunity had been welcomed. Therefore there was no evidence whatsoever that the frequency, timing and duration of calls had inconvenienced any dermatologist. Representatives had always been careful to comply with the wishes of the dermatologists concerned and the arrangements in place at any particular establishment. In addition, although the supplementary information to the Code stated that the number of calls made on a doctor by a representative each year should not normally exceed three on average, the circumstances of 2006 together with the low contact rate in the previous year were such that additional contacts would be likely to be welcomed and in any case would not exceed three per year on average. The total number of contacts would include meetings and conferences.

Astellas therefore denied breaches of Clauses 15.4 or 2 and was disappointed that this issue should ever have been raised with the Authority.

PANEL RULING

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

The Panel noted that the Skinsense Briefing Document, given to representatives in October 2006, stated 'Your objective is to see your Senior Grade Dermatologists 4 times by December 31 2006'. There was no explanation that, as submitted by Astellas, this was meant to be the number of contacts for the whole year, not just the period October to December. The Panel considered that without further explanation the briefing document advocated a course of action which was likely to breach the Code. A breach of Clause 15.9 was ruled.

The Panel took the complaint as evidence that overcalling had actually occurred and in that regard noted that the complainant had referred to harassment. A breach of Clause 15.4 was ruled.

A ruling of a breach of Clause 2 of the Code was a sign of particular censure and was reserved for such circumstances. The Panel did not consider that the matter warranted such a ruling.

Complaint received	**6 November 2006**
Case completed	**24 January 2007**

PRIMARY CARE TRUST HEAD OF PRESCRIBING v ABBOTT LABORATORIES

Conduct of representative

The head of prescribing at a primary care trust (PCT) complained that a representative from Abbott Laboratories had failed to keep an appointment. The complainant explained that earlier in 2006 the representative had failed to arrive on time for an appointment but had contacted the PCT and the meeting was cancelled and rebooked. However the representative neither kept the second appointment nor explained his failure to attend. The PCT considered that this disregard wasted staff time and failed to meet high standards.

The Panel noted that the parties had different views of the events. The representative in question stated that he had made it clear to the PCT that the second appointment was for him as an employee of a different pharmaceutical company and not an appointment for Abbott. The PCT thought that the second appointment was for an Abbott employee. The Panel considered that in the circumstances Abbott was not responsible for the failure of the representative to keep the second appointment. No breach of the Code was ruled.

The head of prescribing at a primary care trust (PCT) complained that a representative of Abbott Laboratories Limited had failed to keep an appointment.

COMPLAINT

The complainant stated that earlier in 2006 the representative failed to arrive on time for an appointment. To his credit he telephoned the PCT to explain that he was lost and to ask for further directions; unfortunately by the time he reached the offices it was too late to make the meeting worthwhile and so it was cancelled. His attempts to contact the PCT were professional and so the appointment was rebooked for later in the year and the PCT did not consider that a formal complaint was appropriate.

Given the PCT's experiences the first time around, it was somewhat surprised by the representative's failure to attend the second appointment and further surprised that there was no contact to explain what had happened.

The PCT considered that this disregard for the appointment system not only wasted staff time but also failed to meet the high standards it had come to expect of representatives' conduct in performing their business duties.

When writing to Abbott Laboratories, the Authority asked it to respond in relation to Clauses 15.2 and 15.4 of the Code, paying particular attention to the supplementary information to Clause 15.4.

RESPONSE

Abbott noted that the representative in question left the company at the end of June to join another company in a similar role. It was key to know when the initial visit referred to took place, when specifically the future meeting was booked, and for whom it was booked, himself, Abbott or his new company. Indeed it was possible that he made an appointment with the intention of fulfilling it in his new position, or indeed that both incidences occurred with his new company.

Abbott had a comprehensive standard operating procedure (SOP) relating to the representatives' electronic territory management system, which included electronic diaries. Training was conducted on a regular basis. The representative had signed to confirm he had read, understood and would comply with the SOP. All Abbott's representatives were also fully trained on the Code and the expectations Abbott held with regard to their conduct.

Abbott stated that the representative's last recorded call upon the PCT was at the end of June on his last working day with the company. This meeting was recorded in the electronic system; however, no future appointments for this customer were recorded in his electronic diary, nor described during his 'close out' meeting with his manager. There was no reason Abbott could propose why the representative would not enter a future meeting made on behalf of Abbott as the representative was on the system and aware of his compliance responsibility. Naturally such a meeting would have been honoured by his successor in Abbott. As the representative in question was no longer an Abbott employee the company was unable to investigate the matter directly with him.

Abbott wanted to know the exact date of the initial meeting described by the PCT and for whom and when the second appointment was made. Was it made for Abbott or for the representative on behalf of his new company?

Abbott concluded that there was insufficient information provided to rule that it had breached Clauses 15.2 and 15.4 of the Code.

FURTHER INFORMATION FROM THE COMPLAINANT

In response to a request for answers to Abbott's questions the complainant confirmed that the original meeting booked with the representative was for the representative's last working day for Abbott and was somewhat surprised to learn that he had logged this date as a 'call to the PCT' when he failed to attend. On this day he telephoned to say he would be about half an hour late as he was lost. The PCT staff waited for over half an hour and still there was no sign of him. As staff had other commitments, he was informed that he had missed his slot and it would not be possible to complete the meeting with the PCT that day. However, as the representative had tried to let the PCT know he would be late an appointment was rebooked for a later date. The complainant's administrative assistant handled this so the complainant was not aware of exactly when the meeting was rebooked, however he expected that it was before the end of that week. The representative did not tell the PCT that he was changing company and therefore, to its knowledge, an appointment was rebooked with a representative of Abbott.

The complainant learned that the representative was working for another company when he contacted him about the failed meeting later in the year. At this time he asked if he could book a new appointment on behalf of his new employers. The request was declined based upon his previous history of failing to arrive.

FURTHER COMMENTS FROM ABBOTT

Upon receiving the additional information and in order to progress this investigation and to gain a clearer understanding for which company the second appointment was made, Abbott contacted the representative on 4 January 2007. The representative stated that as he knew he was leaving Abbott he thought he had made it clear to the PCT that he had booked the second appointment on behalf of his new employer. Indeed he stated 'why would I make an appointment for Abbott, when I knew I was leaving'. This would explain why the appointment did not appear in his Abbott electronic diary and why it was not highlighted during his 'close out' meeting with his manager. The representative gave details as to why he had failed to attend the second appointment.

Abbott concluded that as stated previously, whilst employed with Abbott the representative was fully trained on the SOP regarding the use of the electronic territory management system. In making the second appointment with the PCT he was clearly doing so for his new employer (a matter the representative considered he had made clear to the PCT), and therefore he did not log it in his Abbott electronic diary.

Abbott stated that it was sympathetic to the complaint, and understood that it was responsible for the activities of its representatives. However in this case the representative clearly intended to use the appointment for his new employer and not for Abbott. Therefore as an ex Abbott employee acting on behalf of his new employer Abbott could not be held responsible for his actions, nor should it be found in breach of Clauses 15.2 or 15.4 of the Code.

PANEL RULING

The Panel noted that the parties had different views of the events. The representative in question stated that he had made it clear to the PCT that the second appointment was for him as an employee of another pharmaceutical company and not an appointment for Abbott. The PCT thought that the second appointment was for an Abbott employee. The Panel considered that in the circumstances Abbott was not responsible for the failure of the representative to keep the second appointment. No breach of Clauses 15.2 and 15.4 of the Code was ruled.

The Panel considered the complainant should be asked if he wished for his complaint to be raised with the representative's new employer as a new case.

Complaint received 9 November 2006

Case completed 2 February 2007

CASE AUTH/1915/11/06

ASTRAZENECA v NOVARTIS

Femara leavepiece and press release

AstraZeneca complained about a Femara (letrozole) leavepiece issued by Novartis. AstraZeneca alleged that claims that Femara offered protection against increased risk in patients with lymph node positive disease were misleading as they reported only the positive aspect of the trial data, without reporting results for women who had lymph node negative disease. Lymph node status was routinely used to define the risk of recurrence in breast cancer once primary treatment had been administered. It was not clear in the leavepiece that there was currently no evidence of Femara's improved efficacy over tamoxifen in patients with lymph node negative disease. Where a medicine was perceived to be more 'potent' in preventing cancer recurrences in 'higher risk' patients ie node positive patients, there could also be a perception that it would have enhanced benefit in lower risk patients, ie node negative patients. Thus, this lack of clarification might encourage use of Femara in not just node positive patients but also in node negative patients. AstraZeneca had anecdotal evidence that certain clinicians and hospital trusts advocated the use of Femara in all patients requiring an aromatase inhibitor, due to perceived improved potency.

AstraZeneca alleged that claims that Femara offered protection against increased risk in patients who had had previous chemotherapy, were similarly misleading. Patients who had chemotherapy as part of their primary treatment were again perceived to be at higher risk of breast cancer recurrence. The most recent data indicated that Femara was no more effective than tamoxifen in women who had not had previous chemotherapy. With reference to the argument above, making claims only on the positive aspects of the data might encourage clinicians to prescribe Femara in groups of patients who might not benefit but might in consequence suffer unnecessarily from serious adverse events.

The Panel considered that claims about Femara and a woman's nodal status clearly referred to data in node-positive women. There was no implication that the data also applied to lymph node-negative disease. The Panel did not accept that in this instance it was misleading to only refer to the positive aspect of the trial. The relevant subgroup analysis was pre-planned. The data for node-negative disease showed no statistically significant difference between tamoxifen and letrozole. The Panel did not consider that the claims in question were misleading as alleged. No breach of the Code was ruled. This ruling was appealed by AstraZeneca.

Similarly the Panel considered that claims about Femara and previous chemotherapy clearly referred to data in patients who had had previous chemotherapy. There was no implication that the data also applied to patients who had not had chemotherapy. The Panel did not accept that in this instance it was misleading to only refer to the positive aspect of the trial. The relevant subgroup analysis was pre-planned. The data for patients who had not had chemotherapy showed no statistically significant difference between tamoxifen and letrozole. The Panel did not consider that the claims in question were misleading as alleged. No breach of the Code was ruled. This ruling was appealed by AstraZeneca.

Upon appeal by AstraZeneca the Appeal Board noted that all of the claims at issue were referenced to the BIG 1-98 study. The results of that study showed that overall disease free survival was significantly greater in the Femara group than in the tamoxifen group (p=0.003). A number of subgroup analyses were performed; the resulting Forest plot showed that the confidence intervals all overlapped a central line demonstrating that none of the subgroups differed significantly from the overall treatment effect in the whole population. No statistical correction had been applied to the results to allow for multiple subgroup analysis.

The first bar chart in the leavepiece at issue showed that for the whole BIG 1-98 study group there was a 19% decrease in recurrences in the Femara group (p=0.003). Two subsequent bar charts showed a 29% decrease in recurrences in node-positive women (p=0.0002) and a 28% decrease in recurrences in those women who had had previous chemotherapy (p=0.02). The differences between 19% and 29% and 28% had been emphasised by proportionately larger downward arrows. The Appeal Board noted its comments above and considered that, given the statistical analysis of the results, there was no way of knowing if the results for the node-positive women and for those who had had previous chemotherapy were truly different from the whole patient population such that there was additional benefit from treatment for these two groups.

The Appeal Board considered that the DFS data from the BIG 1-98 study had been presented in such a way as to imply an increased benefit for Femara in node-positive women and in those who had had previous chemotherapy. Such benefits were unproven. The Appeal Board thus considered that the impression from the leavepiece was misleading as alleged. Breaches of the Code were ruled. The appeal was successful.

AstraZeneca was concerned that there were no safety statements regarding potential serious adverse events within the main body of the leavepiece to provide an

adequate benefit/risk profile of Femara. Although it was claimed that 'Overall FEMARA was generally well tolerated compared with tamoxifen', there were no statements within the leavepiece to clarify what the potential risks were of taking Femara, in particular that women on Femara could anticipate a reduction in bone mineral density, which might increase fracture risk. Given that postmenopausal early breast cancer patients who had received their primary treatment(s) were essentially well, omission of such a potentially serious side effect was misleading.

The Panel noted that the leavepiece did not mention the potential risks of taking Femara. Details of the side effects were given in the prescribing information. The leavepiece stated that 'Overall Femara was generally well tolerated compared with tamoxifen'. The Panel did not consider that the omission of a reference to possible reductions in bone mineral density was such that there was a failure to provide an adequate benefit/risk profile of Femara or that it was misleading as alleged. The Panel ruled no breach of the Code.

AstraZeneca alleged that the claim 'Femara is now the first and only [aromatase inhibitor] licensed for treatment across the entire breast cancer treatment spectrum' in a Novartis press release could not be justified. The word 'entire' was misleading as it could easily be misconstrued as Femara having a marketing authorization for all breast cancer treatment settings which was not so.

The Panel considered that the claim was misleading. Femara was not licensed across the entire breast cancer spectrum; the table of licensed indications in the press release showed that Femara was not licensed for use within five years of surgery, switching from tamoxifen (adjuvant switch). The Panel considered that the press release was thus misleading and not capable of substantiation. Breaches of the Code were ruled.

AstraZeneca UK Limited complained about the promotion of Femara (letrozole) by Novartis Pharmaceuticals UK Ltd. At issue was a leavepiece (ref FEM 05000083). AstraZeneca supplied Arimidex (anastrozole) and Nolvadex-D (tamoxifen).

1 LEAVEPIECE

COMPLAINT

AstraZeneca referred to four claims.

1 'FEMARA - protection against increased risk in specific patient subgroups' followed by a bar chart headed: 'DFS [disease free survival] events in node positive women'.

2 'FEMARA - protection against increased risk in specific patient subgroups' followed by a bar chart headed: 'DFS events in women who had previous chemotherapy'.

3 'FEMARA - for women at increased risk of recurrence eg node-positive and/or previous chemotherapy'.

4 'Overall FEMARA was generally well tolerated compared with tamoxifen'.

AstraZeneca alleged that claims 1 and 3 were misleading as they reported only the positive aspect of the trial data, without reporting results for women who had lymph node negative disease. Lymph node status was routinely used by breast cancer surgeons and oncologists to define the risk of recurrence in breast cancer once primary treatment had been administered and accordingly, lymph node positivity was widely regarded as a predictive factor for a higher risk of cancer recurrence. It had not been made clear within the leavepiece that there was currently no evidence at present of Femara's improved efficacy over tamoxifen in patients with lymph node negative disease. Where a medicine was perceived to be more 'potent' in preventing cancer recurrences in 'higher risk' patients ie node positive patients, there could also be a perception that it would have enhanced benefit in lower risk patients, ie node negative patients. Thus, this lack of clarification might encourage use of Femara in not just node positive patients but also in node negative patients. Already, AstraZeneca had anecdotal evidence that certain clinicians and hospital trust guidelines advocated the use of Femara in all patients requiring an aromatase inhibitor, due to perceived improved potency.

Similarly AstraZeneca alleged in claims 2 and 3 that Femara offered protection against increased risk in patients who had had previous chemotherapy, were misleading as they reported only on the positive aspects of the trial data, without reporting on the most recent trial data for women who did not have chemotherapy. Patients who had chemotherapy as part of their primary treatment were again perceived to be at higher risk of breast cancer recurrence. The most recent data indicated that Femara was no more effective than tamoxifen in women who had not had previous chemotherapy. With reference to the argument above, making claims only on the positive aspects of the data might encourage clinicians to prescribe Femara in groups of patients who might not benefit but might in consequence suffer unnecessarily from serious adverse events.

Breaches of Clauses 7.2, 7.3 and 7.10 of the Code were alleged.

AstraZeneca was concerned that there were no safety statements regarding potential serious adverse events within the main body of the leavepiece to provide an adequate benefit/risk profile of Femara. Although page 4 of the leavepiece claimed that, 'Overall Femara was generally well tolerated compared with tamoxifen', there were no statements within the leavepiece to clarify what the potential risks were of taking Femara. Section 4.4 of the Femara summary of product characteristics (SPC) stated that women on Femara could anticipate a reduction in bone mineral

density, which might increase fracture risk and that bone mineral density assessment should be carried out during treatment. Given that postmenopausal early breast cancer patients who had received their primary treatment(s) were essentially well, omission of such a potentially serious side effect was misleading. Breaches of Clauses 7.2 and 7.10 of the Code were alleged.

In summary the claims were misleading to health professionals due to the unbalanced presentation of the data. There were also insufficient safety statements within the leavepiece to enable a balanced evaluation of the safety/risk profile.

RESPONSE

Novartis noted that the first page of the leavepiece clearly summarised some of the key data from the BIG 1-98 study at an interim analysis published in the New England Journal of Medicine (NEJM). The analysis of data from 8010 women with breast cancer, treated with either tamoxifen or Femara and followed for a median of 25.8 months was that, compared with taxoxifen, adjuvant treatment with Femara reduced the risk of recurrent disease, especially at distant sites.

A number of pre-planned subgroup analyses were also performed at this time point including a comparison of those who had and had not received previous chemotherapy and also a comparison of those women with disease known to have involved lymph nodes with those who had not or whose nodal status was unknown at study entry.

These pre-planned analyses demonstrated that there was a reduced recurrence of disease in patients treated with Femara who had either received previous chemotherapy or who had node positive disease. This difference was statistically significant and when expressed as a hazard ratio, the risk in these groups was 0.77 and 0.71 indicating a reduction in risk of 23% and 29% respectively for women in these groups treated with Femara compared with those treated with tamoxifen. In women who had not received previous chemotherapy or had no nodal disease or unknown nodal status, a statistically significant difference was not seen. However, overall, there was a statistically significant difference between the two treatments in favour of Femara.

In these 'high risk' groups, recurrences were more common and so a reduction in the incidence of recurrence would be more easily seen over this time period. One explanation for the lack of statistically significant difference between the treatments in the 'low risk' (node negative and no prior chemotherapy) groups might be that the lower rate of recurrence overall meant that a difference was harder to demonstrate at this earlier timepoint.

It was important to note that Femara was not suggested to be inferior to tamoxifen with regards to efficacy in the low-risk groups of women in this study and the results suggested that there might even still be an advantage in efficacy, which might have revealed itself had the sample size been greater, as could clearly be seen in the 'Forest plots' in the NEJM paper.

In summary, Novartis believed that the data supported promotion of the use of Femara in these high risk subgroups of node positive women and those who had received previous chemotherapy. Novartis did not accept that it had promoted the use of Femara in women who were node negative or who had not received previous chemotherapy although, unlike some aromatase inhibitors, Femara was licensed in both node positive and node negative disease. It was therefore not unexpected that some clinicians advocated its use in patients regardless of nodal status as observed by AstraZeneca. Finally Novartis did not accept that prescribing Femara instead of tamoxifen in these 'low risk groups' in any way prejudiced patient care. As concluded in the NEJM paper 'our results indicate that Letrozole is an effective option for standard adjuvant therapy, with a relatively favorable safety profile in postmenopausal women with endocrine-responsive breast cancer'.

Novartis disagreed that additional safety statements regarding treatment induced osteoporosis should be included in the leavepiece. This association, as for all common and serious adverse events, was included in the prescribing information. In this particular study, those patients treated with Femara experienced less throboembolic events, lower rate of vaginal bleeding, fewer endometrial biopsies and fewer invasive endometrial cancers than those women treated with tamoxifen. The authors concluded that Femara had a 'relatively favourable safety profile' and so the description of 'well tolerated' was not inconsistent with that.

PANEL RULING

The Panel considered that claim 1 (Femara – protection against increased risk in specific patient subgroups: DFS events in node positive women) and claim 3 (Femara – for women at increased risk of recurrence eg node-positive and/or previous chemotherapy) clearly referred to data in node-positive women. There was no implication that the data also applied to lymph node-negative disease. The Panel did not accept that in this instance it was misleading to only refer to the positive aspect of the trial. The relevant subgroup analysis was pre-planned. The data for node-negative disease showed no statistically significant difference between tamoxifen and Femara. The Panel did not consider that the claims in question were misleading as alleged. No breach of Clauses 7.2, 7.3 and 7.10 was ruled. This ruling was appealed by AstraZeneca.

The Panel considered that claim 2 (Femara – protection against increased risk in specific patient subgroups: DFS events in women who had previous chemotherapy) and claim 3 (Femara – for women at increased risk of recurrence eg node-positive and/or previous chemotherapy) clearly referred to data in patients who had had previous chemotherapy. There was no implication that the data also applied to patients who had not had chemotherapy. The Panel did

not accept that in this instance it was misleading to only refer to the positive aspect of the trial. The relevant subgroup analysis was pre-planned. The data for patients who had not had chemotherapy showed no statistically significant difference between tamoxifen and Femara. The Panel did not consider that the claims in question were misleading as alleged. No breach of Clauses 7.2, 7.3 and 7.10 was ruled. This ruling was appealed by AstraZeneca.

The Panel noted that the leavepiece did not mention the potential risks of taking Femara. Details of the side effects were given in the prescribing information. The leavepiece stated that 'Overall Femara was generally well tolerated compared with tamoxifen'. The Panel did not consider that the omission of a reference to possible reductions in bone mineral density was such that there was a failure to provide an adequate benefit/risk profile of Femara or that it was misleading as alleged. The Panel ruled no breach of Clauses 7.2 and 7.10. This ruling was not appealed.

APPEAL BY ASTRAZENECA

AstraZeneca noted that all three claims related to the use of subgroups as reported in the BIG 1-98 study. AstraZeneca alleged that it was inappropriate and misleading to promote findings of subgroup analyses which took into account sub-populations of the total study population and were distinct from secondary end-point analyses, which analysed different outcomes in the total study population, out of context of the main study. Outlined below were details of the subgroup analyses performed in the BIG 1-98 study and the hazards of misusing subgroup analyses, which in this case misrepresented the views of the study authors. These findings highlighted the need for caution in interpreting subgroup analyses, even in large trials. No subgroups showed significantly different relative efficacy; in particular no significant heterogeneity was observed by nodal involvement status or progesterone receptor status (Coates *et al* 2007).

AstraZeneca noted that the BIG 1-98 study was prospectively designed to assess the benefit of Femara versus tamoxifen in the overall population of breast cancer patients. The primary end point was powered to show an overall effect in DFS and patients were stratified by centre and use of chemotherapy. Therefore the overall objective of this study was not to show benefits in subgroups. It was well accepted that drawing conclusions based on subgroup analyses could be problematic and needed to be placed in context (Altman *et al*, 1996, Mathews *et al* 1996). Altman *et al* highlighted their concerns with this approach stating: 'Exploratory examination of many such subgroups is almost certain to throw up some spurious significant interactions and in practice we cannot tell if a specific interaction is real or spurious'. This concern was also reflected in well-established regulatory guidelines on this issue, the Committee for Proprietary Medicinal Products (CPMP) produced in September 2002 a guidance document for managing multiplicity issues in clinical trials. The Committee emphasised the need for clarification and caution by stating:

'Multiplicity of inferences is present in virtually all clinical trials. The usual concern with multiplicity is that, if it is not properly handled, unsubstantiated claims for the effectiveness of a drug may be made as a consequence of an inflated rate of false positive conclusions. For example, if statistical tests are performed on five subgroups, independently of each other and each at a significance level of 2.5% the chance of finding at least one false positive statistically significant test increases to 12.5%.'

AstraZeneca alleged that the initial publication of the BIG 1-98 study recognised the caution that needed to be applied in these circumstances. Such caution was still required even if such subgroup analyses were pre-planned. The discussion section outlined the different findings in subgroups between the ATAC study (an AstraZeneca study of anastrozole in a similar setting) and the BIG 1-98 study and discussed the fact that the ATAC study subgroup analyses suggested preferential benefits in patients with progesterone receptor negative disease. This finding was, quite rightly, interpreted with caution and had subsequently not been confirmed in other studies. AstraZeneca had therefore not promoted on subgroup data from the ATAC study on this basis. The BIG 1-98 study concluded by clearly stating: 'These findings highlight the need for caution in interpreting subgroup analyses, even in large trials'.

In this case AstraZeneca alleged that it was inappropriate to use subgroup data to infer a treatment benefit and that this contradicted the opinions of the authors. It was also inappropriate to highlight benefits seen in subgroups without clarifying the uncertainty attached to such findings.

Existing evidence (including the BIG 1-98 study data) was reviewed by a recent National Institute for health and Clinical Excellence (NICE) technology assessment on hormonal therapies for the adjuvant treatment of early oestrogen-receptor-positive breast cancer, where it was concluded that:

'However, because of the lack of definitive evidence on the relative clinical and cost effectiveness of the use of the aromatase inhibitors in different risk groups, the Committee did not feel able to issue guidance on the relative cost effectiveness of the aromatase inhibitors for the different subgroups.'

AstraZeneca alleged that these examples confirmed the generally held view that subgroup analyses must be treated with caution and did not provide definitive evidence of a clinical effect.

AstraZeneca submitted that subgroup analyses could be useful in large clinical trials. Analysis could highlight certain patient groups that might be inconsistent with the overall treatment effect. This testing of heterogeneity was well recognised in medical statistics. When used in this way subgroup analysis might be helpful in establishing a hypothesis for

further evaluation. This was a valid and appropriate use of subgroups as outlined by Altman *et al*, Cuzick (2005) and the CPMP guidance. The most recent (51-month median follow up) BIG 1-98 publication clearly outlined this appropriate use of the subgroup analyses:

'We explored various protocol defined subgroups to identify whether there was any apparent difference in the relative efficacy of letrozole on DFS compared with the overall benefit observed. No subgroups showed significantly different relative efficacy; in particular no significant heterogeneity was observed by nodal involvement status or progesterone receptor status (Fig 3B)' (Coates *et al*).

AstraZeneca alleged that it was clear, therefore, that the authors of the BIG 1-98 study did not place clinical importance on the statistically significant finding in the node-positive or chemotherapy group, and indeed had correctly utilised appropriate subgroup analyses to demonstrate that nodal status did not demonstrate heterogeneity. In particular they did not refer to the statistically significant findings in figure 3B, the subgroup table, reflecting only that no subgroups demonstrated heterogeneity. Heterogeneity testing examined whether a treatment worked better in some subgroups compared with others. Although AstraZeneca accepted that this article was published after the original complaint, it further reinforced its original concern around the inappropriate and misleading claims that Novartis had formed from subgroup data. It was therefore, appropriate to introduce this information as further evidence of its concerns.

AstraZeneca submitted that it had provided review articles which clearly outlined how subgroup analyses should be assessed. On the specific issue of node-positive versus node-negative patients, as outlined in its complaint, in order to test for possible interaction in node-positive women, the more appropriate analysis would have been to test for interaction between the node-negative population and the node-positive population. It was this analysis that would determine whether Femara demonstrated efficacy benefits in node-positive women over node-negative women. These analyses had been performed and led to the BIG group to conclude: 'No subgroups showed significantly different relative efficacy; in particular no significant heterogeneity was observed by nodal involvement status or progesterone receptor status'.

AstraZeneca noted the letter from Cuzick, which eloquently outlined the confusions and misinterpretations that occurred from Forest plot analyses and explained how the confusion could arise from misinterpretation of the 'bold line' depicted at the 'no effect' level. The BIG group had correctly utilised the Forest plot to make an appropriate conclusion on the subgroup analysis.

AstraZeneca noted that Novartis had submitted that the analyses were pre-planned. Whilst it was beneficial to pre-plan such analyses it did not exempt them from the issues of multiplicity, as outlined by the CPMP guidance and the articles by Altman *et al*. Furthermore, prospective planning of subgroup analyses did not provide an exemption to carrying out appropriate adjustments such as heterogeneity tests. They also referred to the authors' endorsement of Femara, but did not highlight the authors' concerns around the use of subgroups. Finally, AstraZeneca alleged that Novartis' submission suggesting an explanation for the benefit being observed in high-risk patients where it claimed that 'high-risk' patients' disease recurred earlier and therefore it was easier to show the benefits in these women, further supporting the argument that those apparent differences created by subgroup analyses, did not relate to true clinical differences between subgroups.

In summary, AstraZeneca alleged that the leavepiece was in breach of the Code as it represented selected subgroup analyses as clinical evidence when such analyses were insufficient to provide definitive evidence of a clinical effect and misrepresented the views of the authors.

More specifically:

- The authors of BIG 1-98 clearly highlighted the concerns of subgroup analyses with the statement, 'No subgroups showed significantly different relative efficacy'. The leavepiece was therefore inconsistent with the authors' views.

- The interpretation of the analysis had been misrepresented and dissemination of such information posed the risk of inappropriate conclusions being made by health professionals, which might affect treatment of patients.

- It was inappropriate to conclude from the data, that particular subgroups of patients demonstrated heterogeneity (ie differed from the overall population) within the BIG 1-98 population and to suggest that there were differential benefits for Femara in node-positive patients.

For these reasons, AstraZeneca alleged that it was inappropriate to use subgroup data to make definitive claims of efficacy, and even more so without representing the data in a balanced manner. Therefore the leavepiece breached Clauses 7.2, 7.3 and 7.10.

COMMENTS FROM NOVARTIS

Novartis noted that AstraZeneca continued to assert that promotional claims could not be based on subgroup analyses and that the breaches of the Code it alleged all related to this assertion. Novartis fundamentally disagreed with this and maintained that appropriate use of subgroup analyses provided additional information to prescribers on the activity of a medicine and allowed them to be better informed when deciding on the most appropriate management of their patients.

Novartis noted that the leavepiece was used to reinforce messages following a full and frank discussion with the health professional on the data

contained. The flow of the item first identified the design of the BIG 1-98 study and the primary outcome. Only then was there a discussion of the particular pre-planned subgroup analyses within the context of the main study.

Novartis noted how AstraZeneca had interpreted the CPMP paper, 2002, on the issue of multiplicity issues in clinical trials. AstraZeneca had quoted the opening statement of the guidance that cautioned about the inappropriate use of data generated within clinical trials, without appropriate and robust statistical prior consideration to support claims.

Novartis agreed that 'data dredging' and retrospective analyses to support sophistic arguments could never be condoned. However the paper went on to discuss the analysis of subgroup data according to a pre-defined statistical plan. The guidance stated: 'in general, multiple analyses of varying subsets of subjects or with varying measurements for the purpose of investigating the sensitivity of the conclusions drawn from the primary analysis should not be subjected to adjustment for type 1 error. The main purpose of such analyses was to increase confidence in the results obtained from the primary analysis'.

The paper then went on to specifically discuss where claims could be made from the analysis of secondary variables and stated: 'secondary variables may be related to secondary objectives that become the basis for an additional claim, once the primary objective has been established'.

Novartis submitted that the primary endpoint of the BIG 1-98 study was to compare treatment with Femara and tamoxifen and the effect on DFS. The result of this primary analysis was that DFS was significantly greater in the Femara group than the tamoxifen group (hazard ratio for the primary end point, 0.81; 95 percent confidence interval, 0.70 to 0.93; P = 0.003 by the log-rank test). Therefore with the primary objective established, it was then appropriate and in line with the CPMP guidelines to provide additional granularity by performing pre-planned subgroup analyses.

Novartis submitted therefore that the additional analysis demonstrated that there was a significant improvement in DFS (as demonstrated in a statistically and clinically significant reduction in DFS events in the Femara group when compared with the tamoxifen group) in groups with node-positive disease or who had received prior chemotherapy which was important information for physicians in making management decisions. These groups represented women with more aggressive disease. It was likely that the lack of a demonstrable difference between the treatment arms in those groups with node-negative/unknown disease or who had not received prior chemotherapy was driven by the lower rate of events in either group and that a larger sample size would be needed to show this difference.

Novartis submitted that AstraZeneca had referred to the most recent analysis of data from the BIG-1-98 study, Coates *et al* that was presented at the 2006 meeting of the European Society of Medical Oncology (ESMO) and would be published in the near future. This publication reported a subsequent analysis of a subset of patients from the whole study population at a median follow-up of 51 months. The population considered for this analysis was only around 62% of the total population (4922 out of total of 8028). The paper showed that there was still an improvement in DFS seen in those women treated with Femara over those treated with tamoxifen. In the subgroup analyses this improvement was still seen in the node-positive subgroup (HR 0.77, 95% CI 0.64-0.92) and those women who had received prior chemotherapy (HR 0.74, 95% CI 0.56-0.97). This was consistent with the results seen in the previous analysis of the whole population in the 2005 NEJM paper. The quote regarding lack of heterogeneity referred to the consistency of superiority of Femara over tamoxifen in all subgroups although this was not statistically significant in the node-negative and chemotherapy-naïve groups.

In conclusion Novartis did not accept that the arguments presented by AstraZeneca in relation to the interpretation of subgroup analyses should alter the original ruling. The leavepiece was not in breach of the Code as alleged.

FURTHER COMMENTS FROM ASTRAZENECA

AstraZeneca noted that Novartis had extracted details from the CPMP guidance document it had initially highlighted. In particular Novartis used the wording from section 2.2. AstraZeneca concurred exactly with Novartis' use of this extract. However AstraZeneca was concerned that Novartis had not correctly interpreted this guidance. The paragraph clearly stated: 'The main purpose of such analyses is to increase confidence in the results obtained from the primary analysis'.

AstraZeneca submitted that the CPMP guidance was clear with regard to use of subgroups, which should be analysed to ensure the overall result seen was consistent across different sub-populations, and it had outlined the appropriate interpretation previously.

AstraZeneca further noted and concurred with Novartis' use of a second extract from the CPMP guidance section 3.2, that: 'secondary variables may be related to secondary objectives that become the basis for an additional claim, once the primary objective has been established'.

AstraZeneca was concerned that Novartis had misunderstood and misrepresented this guidance. Section 3.2 related to the use of secondary variables (endpoints). The primary variable for the BIG 1-98 study was DFS. Secondary variables in the BIG 1-98 study were overall survival, systemic disease free survival, and safety. AstraZeneca therefore agreed that Novartis might promote benefits seen for these endpoints, especially as the primary endpoint was achieved. However this paragraph did not relate to subgroups, which were covered in section 4 and they had therefore misrepresented this regulatory guidance.

AstraZeneca agreed that secondary endpoints could be valuable in studies of this nature, but maintained that a different approach was required for subgroups.

AstraZeneca also noted Novartis' rationale for the benefits seen in these two subgroups, and in particular the fact that these patients were high risk and therefore benefits might be seen earlier. A similar study design utilising Arimidex (another aromatase inhibitor) had been published in 2002 (ATAC). The ATAC and BIG 1-98 studies had shown identical benefits in their primary endpoint, DFS. Interestingly, if one extracted subgroups from this study it was women who did not have chemotherapy, and those with node-negative disease, that benefited preferentially. These women were low risk and therefore showed contradictory findings to the BIG 1-98 study. This again highlighted the pitfalls in interpreting subgroups in this way.

Finally AstraZeneca was concerned to see Novartis' misrepresentation of the authors' statement from the 2007 publication. The authors clearly stated: 'No subgroups showed significantly different relative efficacy; in particular, no significant heterogeneity was observed by nodal involvement status or progesterone receptor status'.

Novartis had correctly outlined in its response that: 'The quote regarding lack of heterogeneity refers to the consistency of superiority of Femara over tamoxifen in all subgroups'. In order for this to be the case it could not then be concluded that there were subgroups for whom a greater benefit was observed. By virtue of the statements above the subgroups were showing consistent benefits.

Finally AstraZeneca highlighted an issue with the supposed subgroup benefit. If one followed Novartis' line of reasoning the BIG 1-98 study showed that women with ER-positive disease gained no benefit from Femara and AstraZeneca knew this to be wrong. This further illustrated the pitfalls in interpreting subgroups in this way.

APPEAL BOARD RULING

The Appeal Board noted that all of the claims at issue were referenced to the BIG 1-98 study. The results of that study showed that overall DFS was significantly greater in the Femara group than in the tamoxifen group (p=0.003). A number of subgroup analyses were performed; the resulting Forest plot showed that the confidence intervals all overlapped a central line demonstrating that none of the subgroups differed significantly from the overall treatment effect in the whole population. No statistical correction had been applied to the results to allow for multiple subgroup analysis.

The first bar chart in the leavepiece at issue showed that for the whole BIG 1-98 study group there was a 19% decrease in recurrences in the Femara group (p=0.003). Two subsequent bar charts showed a 29% decrease in recurrences in node-positive women (p=0.0002) and a 28% decrease in recurrences in those women who had had previous chemotherapy (p=0.02). The differences between 19% and 29% and 28% had been emphasised by proportionately larger downward arrows. The Appeal Board noted its comments above and considered that, given the statistical analysis of the results, there was no way of knowing if the results for the node-positive women and for those who had had previous chemotherapy were truly different from the whole patient population such that there was additional benefit from treatment for these two groups.

The Appeal Board considered that the DFS data from the BIG 1-98 study had been presented in such a way as to imply an increased benefit for Femara in node-positive women and in those who had had previous chemotherapy. Such benefits were unproven. The Appeal Board thus considered that the impression from the bar charts and the claims at issue 'Femara - protection against increased risk in specific patient subgroups: DFS events in node-positive women', 'Femara - protection against increased risk in specific patient subgroups: DFS events in women who had previous chemotherapy' and 'Femara - for women at increased risk of recurrence eg node-positive and/or previous chemotherapy' was misleading as alleged. Breaches of Clauses 7.2, 7.3 and 7.10 were ruled in respect of each claim. The appeal was successful.

2 PRESS RELEASE

COMPLAINT

AstraZeneca alleged that the claim 'Femara is now the first and only [aromatase inhibitor] licensed for treatment across the entire breast cancer treatment spectrum - before surgery, directly post-surgery, after five years of standard tamoxifen treatment and in advanced cancer' could not be justified. The word 'entire' was misleading as it could easily be misconstrued as Femara having a marketing authorization for all breast cancer treatment settings. Other aromatase inhibitors such as Arimidex and Aromasin were licensed for the adjuvant treatment of postmenopausal women who had had 2-3 years of initial tamoxifen. However, Novartis did not have a marketing authorization for use of Femara in this setting and thus the claim was not justified. Furthermore, the prescription of aromatase inhibitors after 2-3 years of tamoxifen was an evidence-based treatment strategy that had now been approved by NICE and was therefore not a refinement within the primary adjuvant setting. Health professionals and the public could be misled into thinking that Femara could also be used for this treatment setting. Breaches of Clauses 3.2, 7.2, 7.3, 7.4 and 20.2 of the Code were alleged.

RESPONSE

Novartis disagreed with AstraZeneca's interpretation. The claim referred to the indications which covered the possible uses of an aromatase inhibitor in the treatment of women with breast cancer. Although the use of an aromatase inhibitor in the adjuvant setting after a

period of treatment with tamoxifen had been listed as an additional indication for some aromatase inhibitors, this did not represent a fundamentally different use of these agents. Indeed, the NICE publication divided treatment into 'surgical treatment and adjuvant treatment after surgical removal of the primary cancer'. It described primary adjuvant use and switch therapy as different 'treatment strategies' rather than fundamentally different treatment settings.

The press release clearly presented the licensed indications for the aromotase inhibitors in tabular format leaving the reader in no doubt about the licensed use of the products. In addition the full licensed indications for Femara were listed in the main body of the text.

Femara was the only aromatase inhibitor licensed before surgery, directly post-surgery, after five years of standard tamoxifen treatment and in advanced cancer; therefore it was not unjustified to make this claim.

PANEL RULING

The Panel considered that the claim was misleading. Femara was not licensed across the entire breast cancer spectrum; the table of licensed indications in the press release showed that Femara was not licensed for use within five years of surgery, switching from tamoxifen (adjuvant switch). The Panel considered that the press release was thus misleading and not capable of substantiation. Breaches of Clauses 7.2, 7.3, 7.4 and 20.2 were ruled.

Complaint received	**10 November 2006**
Case completed	**13 March 2007**

PRIMARY CARE TRUST SENIOR PHARMACIST v PFIZER

Promotion of Champix

A senior pharmacist to a primary care trust complained that a presentation on Champix (varenicline) given by a Pfizer representative to the local stop smoking service constituted advance notification as the product was not yet launched. In that regard the complainant noted that the smoking cessation service did not make policy decisions about the entry of new medicines into the local health community nor did it hold budgetary responsibility for such decisions.

The Panel noted that when the presentation was made to the smoking cessation service, Champix had a marketing authorization, albeit that Pfizer had chosen to delay its formal launch. Thus there could be no breach of the Code as alleged and the Panel ruled accordingly.

The senior pharmacist to a primary care trust (PCT) prescribing and management team complained about a presentation on Champix (varenicline) given by a representative of Pfizer Limited to members of the stop smoking service.

COMPLAINT

According to an email from the representative the aim of the presentation was to model the financial and clinical impact of introducing Champix within a defined health economy. Pfizer anticipated a formal launch for Champix in December 2006. The stop smoking service had indicated its wish for Champix to be considered for approval for use within the area. The email sought an appointment with the complainant so that he could have a similar presentation to that already made and it also invited him to a more detailed clinical presentation by the regional medical research specialist.

The complainant stated that the smoking cessation service did not make policy decisions about the entry of new medicines into the local health community nor held budgetary responsibility for such decisions. In this context the complainant was concerned that this activity constituted advance notification which was not allowed under Clause 3.1 of the Code.

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

RESPONSE

Pfizer stated that the European Medicines Evaluation Agency (EMEA) issued a marketing authorization for Champix on 26 September 2006. The regulatory status of Champix was explained at the meeting and attendees were told that, although Champix had received its marketing authorization, Pfizer would not be generating demand or promoting it until after a formal launch.

Pfizer explained that the presentation to the stop smoking service was given in response to an unsolicited request from the service for information on Champix, apparently following requests for information from local general practitioners. The representative who was asked, correctly referred the enquiry to a member of the primary care account management (PCAM) team, who were, amongst their other responsibilities, responsible for informing budget holders about new products prior to launch. The PCAM concerned arranged the meeting and confirmed beforehand that those planning to attend were, as stated by the representative, budget holders for smoking cessation products. Prior to starting the meeting, the PCAM gained confirmation from those present that they were indeed budget holders for smoking cessation products. A list of those present at the meeting was provided.

The PCAM presented the local budget impact model for Champix. A copy of the model with the calculated outcome was provided to the Authority. The PCAM also left a copy of the Champix pre-launch formulary summary for English PCTs and a smoking cessation backgrounder for the head of service, copies of which were also provided.

The complainant suggested that this was advance notification, which was not, in these circumstances in breach of the Code. Champix was licensed at the time of the meeting and so there had been no breach of Clause 3.1.

Pfizer believed that the referral and the presentation and all the materials were appropriate and that Pfizer personnel had acted correctly. Pfizer believed that it was appropriate to make this presentation to these recipients for the reasons stated above.

Therefore Pfizer did not consider that this activity constituted a breach of Clause 9.1 or of Clause 2.

PANEL RULING

The Panel noted that the supplementary information to Clause 3.1 set out the basis upon which information about medicines which were not the subject of

marketing authorizations could be given. At the time that the presentation was made to the smoking cessation service in question, however, Champix had a marketing authorization, albeit that Pfizer had chosen to delay its formal launch. Thus there could be no breach of Clause 3.1 as alleged and the Panel ruled accordingly. It followed that there was also no breach of Clauses 9.1 and 2.

Complaint received **10 November 2006**

Case completed **29 January 2007**

PRIMARY CARE TRUST HEAD OF PRESCRIBING AND MEDICINES MANAGEMENT v PFIZER

Promotion of Champix

The head of prescribing and medicines management at a primary care trust (PCT) complained about the promotion of Champix (varenicline) by Pfizer, referring particularly to an invitation sent by Pfizer to attend a 'new treatment launch update' meeting which she believed breached the spirit if not the letter of the Code.

The complainant was concerned that materials devised for GPs were not suitable for NHS administrative staff. Specialists in smoking cessation came from a wide variety of backgrounds, but most were not members of regulated health professions, and in that respect might be considered to be managerial or administrative staff. These individuals were not able to interpret the content of the draft summary of product characteristics (SPC) which had been attached with the invitations, or to apply its content (for instance in respect of renal impairment etc) in any discussions with members of the public.

It was clear from the invitation that the true purpose of the meeting was to prime smoking cessation advisers to encourage members of the public to ask their doctors or other prescribers to prescribe Champix. The complainant believed this was a clear breach of the Code.

The Panel noted that the Code applied, *inter alia*, to the promotion of medicines to members of the UK health professions and to appropriate administrative staff. Health professionals included members of the medical, dental, pharmacy and nursing professions and any other persons who in the course of their professional activities might prescribe, supply or administer a medicine. Appropriate administrative staff were not defined in the Code but advice about promotion to them was given in the supplementary information.

The meetings were arranged at the request of the regional tobacco policy manager, who had also selected the attendees. The Panel did not accept Pfizer's contention that, together with the job titles of the delegates, such a selection process was more than adequate justification for their attendance. Irrespective of the involvement of the regional tobacco policy manager Pfizer was responsible for ensuring that the arrangements including the selection of invitees complied with the Code. The Panel noted that a broad group of individuals were invited to attend the meeting, including employees and advisors of all Stop Smoking Service contacts in the region. The Panel noted Pfizer's estimate that 95% of attendees at the first meeting qualified as health professionals in that they were 'involved in seeing patients involved in giving up smoking'. However, the Panel noted that such individuals did not, in the course of their professional activities, prescribe, supply or administer a medicine and thus did not meet the definition of a health professional in the Code.

The Panel noted that the attendees were part of, or very closely linked to, services to support smoking cessation. Roles would vary but many of the attendees would be involved in giving advice and information about medicines either to those trying to stop smoking or to health professionals. The Panel considered that in these circumstances it was not unreasonable to provide clinical information to the attendees who if not health professionals would be appropriate administrative staff. The presentations used at the meeting had been developed specifically to meet the needs of the audience. The material did not advertise a prescription only medicine to the general public. It was not inappropriate to advertise Champix to the attendees. No breach of the Code was ruled.

The head of prescribing and medicines management at a primary care trust (PCT) complained about the promotion of Champix (varenicline) by Pfizer Limited.

COMPLAINT

The complainant referred to an invitation sent by Pfizer to attend a 'new treatment launch update' meeting which she believed breached the spirit if not the letter of the Code.

The complainant was concerned that materials devised for GPs were not suitable for NHS administrative staff. Specialists in smoking cessation came from a wide variety of backgrounds, but most were not members of regulated health professions, and in that respect might be considered to be managerial or administrative staff. These individuals were not able to interpret the content of the draft summary of product characteristics (SPC) which had been attached with the invitations, or to apply its content (for instance in respect of renal impairment etc) in any discussions with members of the public.

The invitation made clear that the true purpose of the meeting was so that smoking cessation advisers could be primed for the purpose of encouraging members of the public to ask their doctors or other prescribers to prescribe a specific prescription only medicine (Champix). The complainant believed this was a clear breach of Clause 20.2 of the Code.

When writing to Pfizer, the Authority asked it to respond in relation to Clauses 2, 9.1 and 12.1 of the Code in addition to Clause 20.2 as referred to by the complainant.

RESPONSE

Pfizer stated that the invitation for this regional meeting was sent out on 3 November 2006. Champix had received its marketing authorization on 26 September 2006.

The intended audience for the meeting, as stated on the invitation, was NHS Stop Smoking Services staff and other interested stakeholders in smoking cessation, specifically pharmacists, doctors and nurses who were responsible for providing smoking cessation advice and services in the region. The NHS Stop Smoking Services were staffed by trained personnel, nurses and pharmacists. The Statistics on NHS Stop Smoking Services in England, April to June 2006, stated:

'The NHS Stop Smoking Services were set up in Health Action Zones in 1999/00 and rolled out across all Health Authorities in England in 2000/01. The services offer support to help people quit smoking. This can include intensive support through group therapy or one-to-one support. The support is designed to be widely accessible within the local community and is provided by trained personnel such as specialist smoking cessation advisers, trained nurses and pharmacists. The services complement the use of smoking cessation aids Nicotine Replacement Therapy (NRT) and bupropion (Zyban).'

Specifically, the invitation was sent to all Stop Smoking Services contacts in the region, including their employees/advisers, ie administrative staff, the 'alliance leads' and the Smoking in Pregnancy Network. At the first meeting on 30 November, there were 47 attendees after 54 had accepted the invitation. From the list Pfizer estimated that 95% of the attendees were health professionals in that they were involved in seeing patients involved in giving up smoking. Pfizer considered therefore that this was a valid group of health professionals to be in receipt of the presentations. Copies were provided. Pfizer explained that the varenicline clinical overview was similar to a presentation made to smoking cessation advisors at a recent advisory board and had been tailored to the intended audience in response to feedback from that meeting. The presentation by a GP represented his own views. The content was devised as a result of discussion between himself and Stop Smoking Services. Pfizer had had no editorial control over the content other than to ensure it complied with the Code.

Pfizer believed therefore that the meetings and the materials complied with the Code. The invitation did not, as the complainant alleged, make it clear that the 'true purpose of the meeting is so that smoking cessation advisers can be primed "for the purpose of encouraging members of the public to ask their doctors or other prescribers to prescribe a specific prescription only medicine (Champix)"'. On the contrary, Pfizer maintained that the invitation and the materials presented were developed specifically to place varenicline appropriately in the context of antismoking treatment modalities. Furthermore, as the meetings were designed for and given to health professionals and their appropriate administrative colleagues, Pfizer strongly refuted the complainant's accusation. Pfizer denied, therefore, any breach of Clause 20.2.

Pfizer believed that the invitation was distributed to a highly relevant category of recipients whose need for and interest in this topic and the information given could reasonably be assumed. High standards had been maintained in the development of these materials and in the preparation of the meetings. Pfizer asserted that nothing had occurred in the context of these meetings that could be construed as bringing discredit upon, or reducing confidence in, the pharmaceutical industry. Pfizer was confident that these meetings and materials did not breach Clauses 2, 9.1 or 12.1.

In response to a request for further information Pfizer provided copies of the delegate list for the meetings with the requested status and role of each attendee. Pfizer noted that from the designations of the attendees set out in this list, at least 95% of the attendees qualified as health professionals under Clause 1.4 of the Code as they consulted with patients who were giving up smoking and might 'prescribe, supply or administer a medicine'. The remaining few attendees were appropriate NHS administrative staff with a relevant interest in smoking cessation therapy, for whom provision was made under Clause 1.1 of the Code.

Pfizer did not have access to details of the qualifications and training of individual attendees. Indeed, it was not Pfizer's standards practice to seek the definition of (or supporting evidence for) the qualifications or training background of health professionals or appropriate administrative staff. Pfizer believed that the job titles of the attendees, as well as the fact that they were selected as appropriate attendees by the regional tobacco policy manager (RTPM), a senior public officer with responsibility for implementation of the Department of Health Stop Smoking Policy, was more than adequate justification for their attendance.

By way of further background, these meetings were arranged at the request of the RTPM to provide a medical presentation on varenicline to frontline staff involved in the provision of smoking cessation advice to patients. Suitable invitees were identified. This list was then scrutinised and approved. Invitations were then sent out by the RTPM. It was understood by Pfizer and the RTPM that invitees, as NHS Stop Smoking Services staff, would be involved in the provision of smoking cessation advice, including advice on and provision of medication to support smoking cessation, and they therefore fulfilled the definition of health professional given in Clause 1.4 of the Code. The invitation was also extended (at the discretion of the RTPM) to invitees outside of the NHS Stop Smoking Services who provided similar smoking

cessation services, including pharmacists, GPs, and in this case, the Smoking in Pregnancy Network. The invitations were approved via the Pfizer promotional approval process, and it was clear that the invitation was intended only for 'frontline' staff seeing patients.

PANEL RULING

The Panel noted that the Code applied, *inter alia*, to the promotion of medicines to members of the UK health professions and to appropriate administrative staff (Clause 1.1). Clause 1.4 explained that a health professional included members of the medical, dental, pharmacy and nursing professions and any other persons who in the course of their professional activities might prescribe, supply or administer a medicine. Appropriate administrative staff were not defined in the Code but advice about promotion to them was given in the supplementary information to Clause 1.1 Promotion to Administrative Staff.

The Panel noted that the meetings were arranged at the request of the RTPM, who had also selected the attendees. The Panel did not accept Pfizer's contention that, together with the job titles of the delegates, such a selection process was more than adequate justification for their attendance. Irrespective of the involvement of the RTPM Pfizer was responsible for ensuring that the overall arrangements including the selection of invitees complied with the Code. The Panel noted that a broad group of individuals were invited to attend the meeting including employees and advisors of all Stop Smoking Service contacts in the region. The Panel noted Pfizer's estimate that 95% of attendees at the first meeting on 30 November qualified as health professionals in that they were 'involved in seeing patients involved in giving up smoking'. However, the Panel noted that such individuals did not, in the course of their professional activities, prescribe, supply or administer a medicine and thus did not meet the definition of a health professional set out in Clause 1.4.

The Panel noted Pfizer's submission that invitees would be involved in the provision of smoking cessation advice. The Panel considered that staff supporting patients on medication within the context of smoking cessation might qualify as appropriate administrative staff under Clause 1.1 of the Code. The Panel noted that the meeting on 30 November included an administrator and a marketing and service development manager. Similarly, the meeting on 8 December included an administrator, an administration manager and a co-ordinator. The status of one delegate, was not stated. Health professionals also attended. The Panel noted that whilst those involved in health administration etc in certain circumstances could qualify as appropriate administrative staff, promotional material had to be relevant to their role; for example, practice managers could attend a company presentation on practice management.

The Panel noted that one presentation, entitled 'Smoking Cessation Efficacy and Safety of an α4ß2 Nicotinic Acetylcholine Receptor Partial Agonist: Varenicline Tartrate' discussed in detail varenicline's mechanism of action, detailed clinical data, including comparative data, a patient support programme and ongoing clinical studies. The Panel noted Pfizer's submission that this presentation had been tailored to the audience after a similar one had been shown to smoking cessation advisors at an advisory board. The second presentation 'Working with varenicline in practice' primarily discussed how to ensure delegates' PCTs had sufficient clinical and financial information to make funding decisions. Two slides discussed the management of clients' expectations of new treatments with reference to varenicline. One slide discussed general practices working with the NHS Stop Smoking Services. The content of this presentation had been devised as a result of discussions between the presenter and Stop Smoking Services.

The Panel noted that the attendees were part of, or very closely linked to, services to support smoking cessation. Roles would vary but many of the attendees would be involved in giving advice and information about medicines either to those trying to stop smoking or to health professionals. The Panel considered that in these circumstances it was not unreasonable to provide clinical information to the attendees who if not health professionals would be appropriate administrative staff. The presentations used at the meeting had been developed specifically to meet the needs of the audience. Thus the Panel ruled no breach of Clause 12.1. The material did not advertise a prescription only medicine to the general public. It was not inappropriate to advertise Champix to the attendees. Thus no breach of Clause 20.2 was ruled.

Given its rulings of no breach the Panel did not consider that Pfizer had failed to meet high standards and no breach of Clause 9.1 was ruled.

Complaint received 15 November 2006

Case completed 20 February 2007

RETIRED HOSPITAL DOCTOR v SCHERING HEALTH CARE

Advertisement to the public about contraception

A retired hospital doctor complained about an advertisement for long-acting reversible contraception (LARC) placed by Schering Health Care in the Marks and Spencer magazine, Christmas 2006. The page was headed 'Advertisement Promotion' and 'Time for you to take control' and discussed contraceptive issues for working mothers. A highlighted box in the bottom right hand corner discussed four methods of LARC; intrauterine system (IUS), intrauterine device (IUD), implant or injection. All except the IUD released progestogen.

The complainant stated that she had never seen an advertisement for progestogens in the medical press which did not include warnings of side effects and special precautions. The advertisement at issue had no warning that progestogens were internationally recognised as carcinogenic and genotoxic.

The complainant was both surprised and alarmed to see the advertisement.

The Panel noted that the complainant had implied that the material was misleading with respect to the safety of LARC because it did not refer to warnings and side-effects related to progestogens. The Panel noted, however, that the material did not refer at all to the safety of LARC. There was no implication that such contraceptive methods had no side-effects. Readers were told that their doctor or family planning nurse could advise them on the most suitable method of contraception for them. On the basis of the complaint made the Panel ruled no breach of the Code.

A retired hospital doctor complained about an advertisement for long-acting reversible contraceptive methods placed by Schering Health Care Limited in the Marks and Spencer magazine, Christmas 2006. The page was headed 'Advertisement Promotion' and 'Time for you to take control' and discussed contraceptive issues for working mothers. A highlighted box in the bottom right hand corner discussed four types of long-acting reversible contraceptive methods; intrauterine system (IUS), intrauterine device (IUD), implant or injection. All except the IUD released progestogen.

COMPLAINT

The complainant stated that she had never seen an advertisement for progestogens in the medical press which did not include warnings of side effects and special precautions. The Marks and Spencer advertisement had no warning that progestogens were recognised by the International Agency for Research on Cancer (IARC), part of the World Health Organization (WHO), as carcinogenic and genotoxic.

The complainant was both surprised and alarmed to see the advertisement.

When writing to Schering Health Care, the Authority asked it to respond in relation to Clauses 2, 9.1 and 20.2 of the Code.

RESPONSE

Schering Health Care submitted that the advertisement was not a 'promotional' piece for any specific product and did not mention any products by name. The heading 'Advertisement Promotion' was included at the insistence of Marks and Spencer to ensure compliance with the British Code of Advertising, Sales Promotion and Direct Marketing 2005 which stated that 'Marketers and publishers should make clear that advertisement features are advertisements, for example by heading them "advertisement feature"'. The piece was in fact a non-promotional health information piece.

Schering Health Care explained that the guidelines from the National Institute for Health and Clinical Excellence (NICE) on long-acting reversible contraception (LARC) recommended that all women should be offered long-acting reversible contraceptives as a choice when they came to consider their family planning needs and this was linked to clear public health goals aiming to reduce unwanted pregnancies. The NICE guidelines stated that in 2003/4 in the UK there was very low uptake of LARC at around 8% of conceptive usage, compared with 25% for the oral contraceptive pill and 23% for the barrier method among women aged 16 to 49. Expert clinical opinion was that LARC methods might have a wider role in contraception and their increased uptake would reduce unintended pregnancy. In 2006, a survey of 100 women currently either taking the combined oral contraceptive pill or the progestogen only pill showed that between 24% and 88% were aware of different LARC methods and only 22% were aware of all four.

The material in question profiled LARC as recommended by the NICE guidelines. The article was written with the aim of informing consumers about the various methods of LARC available, so that they could then have an informed discussion with the relevant health professional. It was not a promotional piece. The piece did not just mention the progestogen implants, injections and IUS but mentioned all long-acting reversible methods of contraception including the

intrauterine device (IUD). The title 'Advertisement Promotion' was added by Marks and Spencer and was not part of the submitted piece which was a general information piece.

As it was unlikely that consumers would understand the methods implied by the term 'long-acting reversible contraception', there was a small informative section on each method of LARC. There was a clear statement at the bottom of the page that indicated where further information could be found (www.modernmotherhood.co.uk which was a non-promotional informative website which had detailed information available on all methods including any warnings, side effects and precautions) and a clear recommendation that a woman's doctor or family planning nurse could advise on the most suitable method of contraception for each women.

Schering Health Care was not aware of any requirement nor any rational argument for the inclusion of the data published by the WHO/IARC (2005) in such a piece. These data concerned the carcinogenicity of estrogen-progestogen replacement therapy and combined oral contraceptives and concluded that the combinations were on the one hand carcinogenic to humans, but that at the same time, there was also convincing evidence for a protective effect of combined oral contraceptives against some other types of cancer. The IARC summarised that 'the overall net public health outcome could be beneficial' for combined oral contraceptives and hormone replacement therapy but that a rigorous analysis would be required to demonstrate this. The WHO regularly reviewed the safety of combined oral contraceptives and assessed the balance of risks and benefits of their use and it had determined that for most healthy women, the health benefits clearly exceeded the risks. Regardless of these findings, the results of WHO/IARC were not generalisable to LARC methods, none of which contained a combination of estrogen and progestogen. Therefore Schering Health Care did not accept that the inclusion of such data in this piece was either warranted or appropriate.

Schering Health Care noted that the Code allowed non-promotional information about prescription only medicines to be provided to the public provided that it was balanced, factual and not made for the purpose of encouraging members of the public to ask their doctors or other prescribers to prescribe a specific prescription only medicine. The material in question was a non-promotional health awareness campaign that highlighted LARC to raise awareness among women as this had been shown to be lacking. This was in line with the NICE LARC guideline that had been published recently with the aim of reducing unwanted pregnancies. The article was of a high standard, including a section by a well respected women's health specialist. The section on the methods available was non-promotional, balanced, fair and accurate and directed women to appropriate places for further information such as a relevant health professional or a factual and balanced website that had extensive information on all methods available. No products were mentioned by brand name and there were no promotional claims made about any products. As such, no information such as prescribing information which included warnings of side effects and special precautions would be expected to be included with such a piece.

Schering Health Care submitted that the material complied with Clauses 20.2, 9.1 and 2 of the Code as a non-promotional health information piece that was of a high standard, was balanced, fair and accurate.

PANEL RULING

The Panel noted that the complainant had implied that the material was misleading with respect to the safety of LARC because it did not refer to warnings and side-effects related to progestogens. The Panel noted, however, that the material did not refer at all to the safety of LARC. There was no implication that such contraceptive methods had no side-effects. Readers were told that their doctor or family planning nurse could advise them on the most suitable method of contraception for them. On the basis of the complaint made the Panel ruled no breach of Clause 20.2. It thus followed that there was no breach of Clauses 2 and 9.1 and the Panel ruled accordingly.

During its consideration of this case, the Panel was concerned that the highlighted box of text which detailed the various LARC methods available gave more positive data about the IUS than the other methods and that in that regard the material was not balanced. Some women might be encouraged to ask their doctor or other health professional for an IUS. The Panel noted that Schering Health Care marketed an IUS - Mirena.

The Panel was further concerned that one part of the website www.modernmotherhood.co.uk which featured patient profiles only profiled women who had been successfully prescribed an IUS. The Panel was concerned that the website was not balanced and that its content would encourage readers to ask their doctor or other health professional to prescribe Mirena.

The Panel decided to take its concerns up as a separate complaint in accordance with Paragraph 17 of the Constitution and Procedure (Case AUTH/1936/12/06).

Complaint received **23 November 2006**

Case completed **16 February 2007**

GENERAL PRACTICE PHARMACIST PRACTITIONER v BRISTOL-MYERS SQUIBB and SANOFI-AVENTIS

Aprovel and CoAprovel mailing

The pharmacist practitioner at a general practice complained about a GP mailing for Aprovel (irbesartan) and CoAprovel (irbesartan and hydrochlorothiazide) sent by Bristol-Myers Squibb and Sanofi-Aventis.

The complainant was concerned about the bold heading 'Treat BP to target today…reduce CV [cardiovascular] risk tomorrow'. There were several referenced claims about the superiority of Aprovel over other angiotensin receptor blockers in terms of BP reduction; however there was no substantiation that either Aprovel or CoAprovel reduced cardiovascular risk and as far as the complainant was aware there was no robust evidence to back that claim.

The complainant also referred to the un-referenced claim 'Aprovel's power to lower blood pressure can help reduce cardiovascular risk in patients with additional risk factors'. This claim might be referring to a post-hoc analysis of the irbesartan diabetic nephropathy trial (Berl *et al* 2005); however this study appeared to conclude that, in diabetics treated with irbesartan, there were reductions in the risk of strokes and of renal failure but there was a statistically significant increase in the risk of heart attack and a non significant increase in heart failure! This could hardly be reported as helping to reduce cardiovascular risk. Additionally, the authors were cautious to highlight that their conclusions were based upon observational data and therefore recommended that a properly conducted randomised study was needed to clarify the treatment guidelines they proposed.

In the Panel's view the layout and content of the piece was such that all of the claims therein would be assumed to be linked to Aprovel and CoAprovel. There was no clear differentiation of general claims about blood pressure and cardiovascular risk from specific claims for Aprovel and CoAprovel.

The Panel noted that Aprovel and CoAprovel were both indicated for the treatment of essential hypertension. Aprovel was also indicated for the treatment of renal disease in hypertensive patients with type 2 diabetes. A benefit of lowering blood pressure would be a reduction of cardiovascular risk but neither medicine was indicated to reduce cardiovascular risk.

The claim 'Treat BP to target today … reduce CV risk tomorrow' appeared halfway down a page of text and immediately below, and to the left, of the product logos for Aprovel and CoAprovel. Every other claim on the page referred specifically to Aprovel and/or CoAprovel. The Panel considered that, in the context in which it appeared, the claim in question implied that Aprovel and CoAprovel, by treating BP to target, reduced cardiovascular risk. There was no data for Aprovel and CoAprovel in this regard. The Panel considered that the claim was misleading and could not be substantiated. Breaches of the Code were ruled.

The claim 'Aprovel's power to lower blood pressure can help reduce cardiovascular risk in patients with additional risk factors' was on a separate page to the claim considered above. The Panel noted that Aprovel was indicated for renal disease in hypertensive type 2 diabetic patients as part of an antihypertensive drug regimen. Aprovel was thus licensed for use in patients with additional risk factors but there was no direct clinical evidence to show that treatment with Aprovel reduced cardiovascular risk in that patient group. The claim was thus misleading and could not be substantiated. Breaches of the Code were ruled.

The pharmacist practitioner at a general practice complained about a GP mailing (ref APR 06/2319) for Aprovel (irbesartan) and CoAprovel (irbesartan and hydrochlorothiazide). Aprovel and CoAprovel were co-promoted by Bristol-Myers Squibb Pharmaceuticals Ltd and Sanofi-Aventis and the matter was taken up with both companies.

COMPLAINT

The complainant was concerned about a bold heading in the centre foldout area that stated, 'Treat BP to target today…reduce CV [cardiovascular] risk tomorrow'. Throughout the document there were several referenced claims about the superiority of Aprovel over other angiotensin receptor blockers in terms of BP reduction; however there was no substantiation that either Aprovel or CoAprovel reduced cardiovascular risk and as far as the complainant was aware there was no robust evidence to back that claim.

The complainant also referred to another un-referenced claim in the first gate foldout section that stated 'Aprovel's power to lower blood pressure can help reduce cardiovascular risk in patients with additional risk factors'. This claim might be referring to a post-hoc analysis of the irbesartan diabetic nephropathy trial (Berl *et al* 2005); however this study appeared to conclude that, in diabetics treated with irbesartan, there were reductions in the risk of strokes and of renal failure but there was a statistically significant increase

in the risk of heart attack and a non significant increase in heart failure! This could hardly be reported as helping to reduce cardiovascular risk. Additionally, the authors were cautious to highlight that their conclusions were based upon observational data and therefore recommended that a properly conducted randomised study was needed to clarify the treatment guidelines they proposed.

When writing to the companies, the Authority asked them to respond in relation to Clauses 7.2 and 7.4 of the Code.

RESPONSE

In a joint response the companies noted that no mention of Aprovel or CoAprovel was made within the claim 'Treat BP to target today … reduce CV risk tomorrow' which reflected the widely understood medical and scientific fact that patients with elevated blood pressure were at greater risk of cardiovascular events. This was the basis of antihypertensive treatments and the conclusion of a substantial body of evidence that the reduction of blood pressure would reduce cardiovascular risk.

The claim therefore also reflected widely accepted, current national and international recommendations for the prevention of cardiovascular disease. The Joint British Societies' guidelines, second revision (2005) were one such example and were referred to in the mailing. These stated: 'The object of CVD prevention in these high risk people is the same - namely, to reduce the risk of a non-fatal or fatal atherosclerotic cardiovascular event and to improve both quality and length of life. This can be achieved through lifestyle and risk factor interventions and appropriate drug therapies to lower blood pressure, modify lipids, and reduce glycaemia. We have set targets (see below) for lifestyle, blood pressure, lipids, and glucose for these high risk people'.

The claim 'Treat BP to target today…. reduce CV risk tomorrow' therefore supported the current medical approach of reducing BP, particularly to recommended targets, to reduce a hypertensive patient's cardiovascular risk. The claim clearly referred to the effect on cardiovascular risk of BP lowering per se, rather than that of any specific medicine. This was distinct from specific claims elsewhere on this item which referred only to the effect of Aprovel and CoAprovel on blood pressure and not to any clinical outcome or cardiovascular risk reduction by direct linkage. Hence, no claim was made for a direct benefit of Aprovel or CoAprovel on cardiovascular risk. Equally, there was substantial and current evidence as described above, for the claim which directly linked BP treatment with reduction in cardiovascular risk.

The companies therefore did not believe that the claim was in breach of Clause 7.2 or 7.4.

The companies submitted that the claim 'Aprovel's power to lower blood pressure can help reduce cardiovascular risk in patients with additional risk factors' was not taken from Berl *et al*. In fact the claim was, again, in support of the guidelines that advocated reducing BP to target in order to reduce cardiovascular risk, described above and positioned adjacent to the claim.

Although the claim was not referenced, it referred to one of the main licensed indications for Aprovel (clearly visible to the left of the claim upon opening the mailing) - that was the treatment of hypertensive patients with type 2 diabetes and renal disease. As the claim did not refer to published studies, it was not mandatory to cite references provided that the requirements of Clauses 7.2 and 7.4 were met.

The mailing clearly identified several studies that supported the ability of both Aprovel and CoAprovel to reduce BP. By lowering BP to target, patients could be helped to reduce their cardiovascular risk, as claimed.

Again, the companies considered that these factors confirmed that there had been no breach of Clauses 7.2 and 7.4 of the Code in respect of this claim.

In summary, the companies submitted that the evidence was clearly reflected and substantiated to demonstrate that the information, claims and comparisons used were accurate, balanced, fair and not misleading.

PANEL RULING

The Panel noted that the claims in question were contained in a short promotional mailing for Aprovel and CoAprovel. In the Panel's view the layout and content of the piece was such that all of the claims therein would be assumed to be linked to the two products. There was no clear differentiation of general claims about blood pressure and cardiovascular risk from specific claims for Aprovel and CoAprovel.

The Panel noted that Aprovel and CoAprovel were both indicated for the treatment of essential hypertension. Aprovel was also indicated for the treatment of renal disease in hypertensive patients with type 2 diabetes. A benefit of lowering blood pressure would be a reduction of cardiovascular risk but neither medicine was indicated to reduce cardiovascular risk.

The claim 'Treat BP to target today … reduce CV risk tomorrow' appeared halfway down a page of text and immediately below, and to the left, of the product logos for Aprovel and CoAprovel. Every other claim on the page referred specifically to Aprovel and/or CoAprovel. The Panel considered that, in the context in which it appeared, the claim in question implied that Aprovel and CoAprovel, by treating BP to target, reduced cardiovascular risk. There was no data for Aprovel and CoAprovel in this regard. The Panel considered that the claim was misleading and could not be substantiated. Breaches of Clauses 7.2 and 7.4 were ruled.

The claim 'Aprovel's power to lower blood pressure

can help reduce cardiovascular risk in patients with additional risk factors' was on a separate page to the claim considered above. The Panel noted that Aprovel was indicated for renal disease in hypertensive type 2 diabetic patients as part of an antihypertensive drug regimen. Aprovel was thus licensed for use in patients with additional risk factors but there was no direct clinical evidence to show that treatment with Aprovel reduced cardiovascular risk in that patient group. The claim was thus misleading and could not be substantiated. Breaches of Clauses 7.2 and 7.4 of the Code were ruled.

Complaint received **4 December 2006**

Case completed **12 February 2007**

CASE AUTH/1926/12/06

GENERAL PRACTITIONER v LILLY

Unsolicited provision of samples

A general practitioner complained about samples of Cialis (tadalafil), a Lilly product, which he had received by post from an agency. He had not requested them and had they been sent to him by a pharmaceutical company they would have been in breach of the Code.

Correspondence provided by the complainant indicated that the agency had told him that it had signed sample requests from three of the doctors in the practice, including the complainant, but that the complainant contended that none of the signatures were those of the doctors concerned.

The Panel noted that the Lilly representative, when collecting the signed sample request forms, dated them, completed the address details and confirmed with the practice receptionist which sample request form related to which doctor. The complainant stated that the signatures on the sample request forms were not his or those of his GP colleagues. Lilly was satisfied that the signatures were made before the sample request forms were collected by the representative. Lilly stated that it had told the complainant about this and asked that the matter be investigated. The Panel noted that the completed sample request forms each bore a different signature.

The Code required sample request forms to be both signed and dated. The supplementary information referred to preprinted sample request forms that had been signed and dated by the applicant. Contrary to the requirements, the forms had been undated when received by the representative who had dated them himself. A breach of the Code was ruled. The Panel was concerned about the overall arrangements but considered in the circumstances that there had not been a failure to maintain high standards.

The Code required that no unsolicited medicine should be sent through the post. The Panel noted that it was not possible to determine precisely who had signed the sample request forms but considered that as far as Lilly was concerned the samples had been requested. Lilly had responded to the requests in good faith. The Panel ruled no breach of the Code in that regard.

A general practitioner complained about samples of Cialis (tadalafil), an Eli Lilly and Company Limited product, which he had received by post.

COMPLAINT

The complainant stated that the samples had been sent to him by an agency rather than by Lilly. He had not requested them and had they been sent to him by a pharmaceutical company they would have been in breach of the Code.

Correspondence provided by the complainant indicated that the agency had told him that it had signed sample requests from three of the doctors in the practice, including the complainant, but that the complainant contended that none of the signatures on them were those of the doctors concerned.

When writing to Lilly, the Authority asked it to respond in relation to Clauses 2, 9.1, 15.2, 17.3 and 17.10 of the Code.

RESPONSE

Lilly explained that its agency provided Cialis samples upon request to GPs and hospital doctors qualified to prescribe it. The sampling process stated that a doctor or specialist could only receive 10 sample packs per year.

Lilly representatives did not carry samples. Samples could only be provided to a health professional if the health professional signed a sample request form, which included the requesting health professional's name, address, date and what split of sample packs was required.

The agency fulfilled all Lilly sample requests and ensured that they were delivered to the correct named person. Before despatching the samples, the agency checked that: the doctor was registered, the doctor had signed the sample request form and that all details had been completed correctly and that no more that 10 samples had been supplied to that doctor that particular year.

The relevant representative visited the complainant's practice in November and left sample request forms for the doctors in the practice to sign if they required Cialis samples. All three doctors had previously attended group-sells in respect of Cialis and were therefore familiar with the product. The representative called back later the same day to pick up the signed sample request forms from reception. The address details were not filled out so the representative completed those himself and confirmed with the receptionist which sample sheet correlated to which doctor, in order to ensure that the sample request forms were appropriately completed before, in accordance with Lilly's sampling standard operating procedure (SOP), sending them to the agency and submitting one other copy to his manager.

Lilly had, as part of this complaint, found out that the

signatures on the sample request forms at issue were not those of the doctors indicated on them. Lilly was satisfied that the signatures were made before the forms were collected by its representative. Neither Lilly nor the agency would therefore have had any reason to believe that the sample request forms were not appropriately requested and in compliance with Clause 17 of the Code. Lilly had subsequently made the doctors at the practice aware of this and requested that the matter be investigated by the practice. Lilly did not know who had made the signatures on the sample request forms but reiterated that Lilly's SOP and consequently the provisions of the Code had been complied with.

In light of the above, Lilly did not believe that Clauses 17.3 and/or 17 10 of the Code had been breached. The samples were provided in response to signed and dated sample request forms. Lilly did not know that the sample requests were not signed by doctors and that the signatures had been forged. The doctors in question had all attended group-sells on Cialis and it was therefore reasonable for Lilly (and its agency) to respond to the signed sample request forms forwarded by the representative. The representative collected the duly signed sample request forms from the practice and had the receptionist explain which request form was signed by which doctor. Lilly considered that it had complied with its SOP in respect of sampling and consequently the Code.

In respect of Clause 15.2 Lilly believed that the representative in question had at all times maintained a high ethical conduct and complied with the Code and Lilly's SOPs. He left sample request forms at the practice to be completed by doctors, if they wanted some samples; he had not insisted on seeing the doctors for this purpose as this might have amounted to undue pressure to gain an interview and knew that the doctors in question knew the product and its profile. The representative had not logged the attendance at the practice as calls on the doctors and had returned to the surgery to collect the signed sample request forms on the same day as leaving them and was informed that they were duly signed and moreover the receptionist identified to the representative which doctor signed which sample request.

In light of Lilly's position in respect of Clauses 17.3; 17.10 and 15.2 set out above, Lilly strongly believed that it had not breached the provisions of Clauses 9.1 and/or 2, ie that high standards had been maintained at all times and that its representative's/ agency's conduct did not bring the industry into disrepute. In light of what was set out above Lilly believed that there was no case for Lilly to answer in this regard and that the Director should therefore determine that there was no *prima facie* case to answer.

The Authority subsequently asked Lilly whether the sample request forms had been dated by the representative, the receptionist or the doctor. In response, Lilly stated that the forms were dated by its representative on the day on which they were collected from the practice.

PANEL RULING

The Panel noted that the Lilly representative, when collecting signed sample request forms from a general practice, dated them, completed the address details and confirmed with the practice receptionist which sample request form related to which doctor. The complainant stated that the signatures on the sample request forms were not his or those of his GP colleagues. Lilly was satisfied that the signatures were made before the sample request forms were collected by the representative. Lilly had made the complainant and the relevant practice aware of this and had requested that the matter be investigated by the practice. The Panel noted that the completed sample request forms each bore a different signature.

The Panel noted that Clause 17.3 required sample request forms to be both signed and dated. The supplementary information to Clause 17.3 referred to preprinted sample request forms that had been signed and dated by the applicant. Contrary to the requirements of Clause 17.3 the forms had been undated when received by the representative who had dated them himself. A breach of Clause 17.3 was ruled. The Panel was concerned about the overall arrangements but considered in the circumstances that rulings of breaches of Clauses 9.1 and 15.2 were not warranted.

Clause 17.10 required that no unsolicited medicine should be sent through the post. The Panel noted that it was not possible to determine precisely who had signed the sample request forms but considered that as far as Lilly was concerned the samples had been requested. Lilly had responded to the requests in good faith. The Panel ruled no breach of Clause 17.10.

The Panel considered that overall the circumstances did not warrant a ruling of a breach of Clause 2 of the Code which was reserved to indicate particular censure.

Complaint received 6 December 2006

Case completed 14 February 2007

DOCTOR v SANOFI PASTEUR MSD

Gardasil journal advertisement

A doctor complained about a double page journal advertisement for Gardasil (Human Papillomavirus Vaccine [Types 6, 11, 16, 18] (Recombinant, adsorbed)) issued by Sanofi Pasteur MSD. Gardasil was licensed, *inter alia*, for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high grade vulvar dysplastic lesions (VIN 2/3), and external genital warts (condyloma acuminata) causally related to human papillomavirus (HPV) types 6, 11, 16 and 18.

The complainant alleged that the claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was still to be proven. Clinical trials had shown that the vaccine was successful in removing transient HPV 16 and 18 infections and might prevent pre-stages to cervical cancer, but no evidence had been seen of final prevention of cervical cancer.

The Panel considered that as Gardasil was licensed, *inter alia*, for the prevention of cervical carcinoma the claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was not misleading nor incapable of substantiation as alleged. No breach of the Code was ruled.

The complainant alleged that the claim 'Benefit from 4 types – before and beyond cervical cancer' was misleading and false. What was known was that HPV types 6 and 11 could cause genital warts but never cervical cancer. Types 16 and 18 together with several other HPV oncogene types could cause cervical cancer, but only if the virus had transformed and started to produce oncogene proteins (E6/E7).

The Panel noted that the claim 'Benefit from 4 types - before and beyond cervical cancer' appeared in a relatively small typeface beneath the bold, prominent claim considered above: 'Now there's Gardasil a vaccine that can prevent cervical cancer' on the first page of the double page spread. The facing second page of the advertisement was headed 'The first vaccine that can prevent cervical cancer' beneath which 2 bullet points discussed the licensed indication of Gardasil and the HPV types 6, 11, 16 and 18. The Panel considered that the claim 'Benefit from 4 types - before and beyond cervical cancer' was ambiguous. Some might consider that the four types referred to HPV types 6, 11, 16 and 18. Given the prominence of the preceding claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' and its reference to cervical cancer some readers might assume that the claim at issue implied that HPV types 6, 11, 16 and 18 each had a role in cervical cancer. It was only by reading the less prominent text in the bullet points on the facing page that the causative effects of the four HPV types became clear. Others might consider that '4' referred to the four licensed indications. On balance, the Panel considered that in the context in which it appeared it was not entirely clear what the claim 'Benefit from 4 types - before and beyond cervical cancer' meant and in this regard it was ambiguous, misleading and incapable of substantiation. Breaches of the Code were ruled.

On appeal by Sanofi Pasteur MSD, the Appeal Board had some concerns that in the claim at issue 'before … cervical cancer' related to time ie high-grade cervical dysplasia whereas 'beyond cervical cancer' related to anatomy ie vulval lesions or external genital warts. However the Appeal Board considered it unlikely that readers would assume that 'beyond' referred to a time after which a woman had developed cervical cancer given that the very prominent claim which preceded the claim at issue clearly referred to the prevention of cervical cancer.

The Appeal Board did not consider that the claim implied that HPV types 6, 11, 16 and 18 all caused cervical cancer as alleged.

Although noting its concern above, the Appeal Board considered that, in the context in which it appeared, the claim was not ambiguous or misleading and could be substantiated. No breach of the Code was ruled.

The complainant alleged that the claim 'Gardasil can also … reduce incidence of vaginal pre-cancers caused by human papillomavirus types 6, 11, 16 or 18' was misleading. It was known that HPV types 6 and 11 could cause genital warts but never cervical cancer. HPV types 6 and 11 could not support the production of oncogene E6 and E7 proteins. Types 16 and 18 together with several other HPV oncogene types could produce oncogene E6 and E7 proteins, the cause of cervical cancer.

The Panel considered that as Gardasil was licensed to prevent high grade vulvar dysplastic lesions (VIN 2/3) the claim 'Beyond the cervix Gardasil can also prevent vulval pre-cancers and genital warts and reduce the incidence of vaginal pre-cancers caused by human papillomavirus types 6, 11, 16 or 18' was not misleading. The phrase 'Beyond the cervix …' made it clear that the claim related to conditions other than cervical cancer. There was no implication that HPV types 6 and 11 caused cervical cancer as inferred by the complainant. No breach was ruled.

The complainant alleged that the claim 'To protect

young women, children and adolescents' was a hanging comparison. The Panel considered that the claim clearly related to Gardasil's licensed indication and no breach of the Code was ruled.

A doctor complained about a double page journal advertisement (ref 10/06 09214c) for Gardasil (Human Papillomavirus Vaccine [Types 6, 11, 16, 18]. (Recombinant, adsorbed)) issued by Sanofi Pasteur MSD Ltd. Gardasil was licensed for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high grade vulvar dysplastic lesions (VIN 2/3), and external genital warts (condyloma acuminata) causally related to HPV types 6, 11, 16 and 18.

COMPLAINT

The complainant asserted that the claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was still to be proven. Clinical trials had shown that the vaccine was successful in removing transient human papillomavirus (HPV) 16 and 18 infections and might prevent pre-stages to cervical cancer, but no evidence had been seen of final prevention of cervical cancer. The vaccine might even make it very difficult for the current screening method to detect underlying pre-stages of cervical cancer.

The complainant alleged that the claim 'Benefit from 4 types – before and beyond cervical cancer' was directly misleading and false. What was known was that HPV types 6 and 11 could cause genital warts but never cervical cancer. Types 16 and 18 together with several other HPV oncogene types could cause cervical cancer, but only if the virus had transformed and started to produce oncogene proteins (E6/E7).

The complainant alleged that the claim 'Gardasil can also … reduce incidence of vaginal pre-cancers caused by human papillomavirus types 6, 11, 16 or 18' was another directly misleading statement. What was known was once again that HPV types 6 and 11 could cause genital warts but never cervical cancer. HPV types 6 and 11 could not support the production of oncogene E6 and E7 proteins. Types 16 and 18 together with several other HPV oncogene types could produce oncogene E6 and E7 proteins, the cause of cervical cancer.

The complainant alleged that the claim 'To protect young women, children and adolescents' was a hanging comparison in breach of the Code.

When writing to Sanofi Pasteur MSD, the Authority asked it to respond in relation to Clause 7.2 and 7.4 of the Code.

RESPONSE

Although Sanofi Pasteur MSD recognised that it did not guarantee compliance with the Code, the advertisements referred to were pre-vetted by the Medicines and Healthcare products Regulatory Agency (MHRA).

Sanofi Pasteur MSD noted that Gardasil was indicated, *inter alia*, to prevent cervical cancer causally related to HPV types targeted by the vaccine (section 4.1 of the summary of product characteristics (SPC)). The claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' therefore reflected the indication - Gardasil could prevent cervical cancer.

Sanofi Pasteur MSD did not consider that the claim 'Benefit from four types – before and beyond cervical cancer' was either misleading or false. It was clear from the SPC that in addition to the prevention of cervical cancer Gardasil was also indicated for the prevention of cervical dysplasia (pre-cancerous lesions that developed before cervical cancer itself), as well as diseases that occurred beyond the cervix (ie vulval intra-epithelial neoplasia, genital warts), all causally related to HPV types targeted by the vaccine. These details were expanded upon in the body of the advertisement. Furthermore Sanofi Pasteur MSD was unsure why the complainant distinguished between types 6 and 11 versus types 16 and 18 since the claim was not just about cervical cancer.

Again, Sanofi Pasteur MSD did not believe that the claim 'Gardasil can also … reduce the incidence of vaginal pre-cancers caused by human papillomavirus types 6, 11, 16 or 18' was either misleading or false. The company was also unsure why the complainant referred to cervical cancer since this claim was not about cervical cancer. The reference to the four HPV types simply reflected section 5.1 of the SPC (sub-section titled 'Efficacy in subjects naïve to the relevant vaccine HPV type(s)') where results for CIN 2/3 or adenocarcinoma in situ (AIS) were related to types 16 or 18 whereas all other results were related to types 6, 11, 16 or 18.

The claim 'To protect young women, children and adolescents' was not a hanging comparison since no comparison was made. In the context of an advertisement for a quadrivalent HPV vaccine, which described the diseases against which the vaccine was effective, it was self-evident what the protection was against. In addition, it reflected the population for which Gardasil was indicated.

Sanofi Pasteur MSD submitted that all of the claims at issue were accurate, balanced, fair, objective and not misleading; all of the claims could be substantiated by the SPC. The company denied any breaches of either Clause 7.2 or 7.4 of the Code.

PANEL RULING

The Panel noted that Gardasil was licensed for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high grade vulvar dysplastic lesions (VIN 2/3), and external genital warts (condyloma acuminata) causally related to HPV types 6, 11, 16 and 18. Section 5.1 of the SPC,

Pharmacodynamic properties, discussed data on the immune response to Gardasil which showed that overall, 99.9%, 99.8%, 99.8% and 99.6% of individuals who received Gardasil became anti-HPV6, anti-HPV11, anti-HPV16 and anti-HPV18 seropositive, respectively, by one month post dose three across all age groups tested. The Panel noted the complainant's submission about treatment of transient HPV infections and their causal link to prevention of pre-stages to cervical cancer but considered that given the product's licensed indication the claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was not misleading nor incapable of substantiation as alleged. No breach of Clauses 7.2 and 7.4 was ruled.

The claim 'Benefit from 4 types - before and beyond cervical cancer' appeared in a relatively small typeface beneath the bold, prominent claim considered above, 'Now there's Gardasil a vaccine that can prevent cervical cancer' on the first page of the double page spread. The facing second page of the advertisement was headed 'The first vaccine that can prevent cervical cancer' beneath which 2 bullet points discussed the licensed indication of Gardasil and the HPV types 6, 11, 16 and 18. The Panel considered that the claim 'Benefit from 4 types - before and beyond cervical cancer' was ambiguous. Some might consider that the four types referred to HPV types 6, 11, 16 and 18. Given the prominence of the preceding claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' and its reference to cervical cancer some readers might assume that the claim at issue implied that HPV types 6, 11, 16 and 18 each had a role in cervical cancer. It was only by reading the less prominent text in the bullet points on the facing page that the causative effects of the four HPV types became clear. Others might consider that '4' referred to the four licensed indications. On balance, the Panel considered that in the context in which it appeared it was not entirely clear what the claim 'Benefit from 4 types - before and beyond cervical cancer' meant and in this regard it was ambiguous, misleading and incapable of substantiation. Breaches of Clauses 7.2 and 7.4 were ruled. This ruling was appealed.

The Panel considered that as Gardasil was licensed to prevent high grade vulvar dysplastic lesions (VIN 2/3) the claim 'Beyond the cervix Gardasil can also prevent vulval pre-cancers and genital warts and reduce the incidence of vaginal pre-cancers caused by human papillomavirus types 6, 11, 16 or 18' was not misleading as alleged. The phrase 'Beyond the cervix …' made it clear that the claim related to conditions other than cervical cancer. There was no implication that HPV types 6 and 11 caused cervical cancer as inferred by the complainant. No breach of Clauses 7.2 and 7.4 was ruled.

The Panel did not consider the claim 'To protect young women, children and adolescents' was a hanging comparison as alleged. It clearly related to Gardasil's licensed indication. No breach of Clause 7.2 was ruled.

APPEAL BY SANOFI PASTEUR MSD

Sanofi Pasteur MSD noted that Gardasil was indicated not just for the prevention of cervical cancer, but also for the prevention of high-grade cervical dysplasia (CIN 2/3) (pre-cancerous lesions that developed before cervical cancer itself), as well as diseases that occurred beyond the cervix (ie high-grade vulvar dysplastic lesions (VIN 2/3) and external, genital warts) all causally related to HPV types targeted by the vaccine (6, 11, 16 and 18). These details were expanded upon in the body of the advertisement.

Sanofi Pasteur MSD submitted that the fact that Gardasil provided protection against four HPV types was clear from the generic name which was displayed in a large font beneath the most prominent mention of the brand name in the top right hand corner of the advertisement. Sanofi Pasteur MSD had never seen the indications for any medicine referred to as 'types'. Therefore four types could only refer to the four virus types covered by the vaccine. So, was the positioning of the claim misleading by implying that the four types might be causal in the development of cervical cancer? Sanofi Pasteur MSD did not believe this to be the case. Despite being in the 'bubble' with the claim about cervical cancer, the reference to four types was immediately qualified after the hyphen - namely that the benefits accrued from the vaccine protecting against four types that occurred before (cervical dysplasia) and beyond (other HPV-related diseases) cervical cancer. Indeed, in its ruling on the third component of the complaint, referring to the body text on the right hand side of the advertisement, the Panel stated that the phrase 'Beyond the cervix …' made it clear that the claim related to conditions other than cervical cancer. This claim did not misleadingly imply that HPV types 6, 11, 16 and 18 were all implicated in the aetiology of cervical cancer. In summary, the claim 'Benefit from 4 types - before and beyond cervical cancer' was neither ambiguous nor misleading and was therefore not in breach of Clause 7.2.

Sanofi Pasteur MSD submitted that regardless of the interpretation of the claim, both the fact that there were benefits from targeting four virus types with Gardasil and the fact that Gardasil had four indications was supported by the SPC. In addition, the fact that the benefits accrued from the vaccine protecting against four types occurred before (cervical dysplasia) and beyond (other HPV-related diseases) cervical cancer was also supported by the SPC. Therefore the claim in question could be substantiated and was not in breach of Clause 7.4.

COMMENTS FROM THE COMPLAINANT

The complainant was astonished and surprised that the response and appeal only referred to the SPC; no publication had been submitted to support the claim at issue.

For information the complainant provided an email

from a professor who he had asked for help and support in this case. The professor had searched the whole medical worldwide database (ENTREZ PUBMED) for any reports about the relationship between HPV6, HPV6b or HPV11 and vulvar dysplastic lesions or high-grade vulvar dysplastic lesions and was unable to find anything. The most important evidence for the causal role between HPV and cancer progression was the binding and degrading by the HPV E6 full-length protein and the p53 tumour suppressor protein. In Hiller *et al* (2006), 'in contrast, the E6 proteins of HPV6 and 11 and HPV44, 54, and 61, regarded as possible carcinogenic or low-risk HPV types, respectively, did not degrade p53'. In Hudelist *et al* (2004), further HPV typing in cervical biopsies of 78 women showed that HPV6 and 11 were restricted to **benign cellular changes**, CIN I and II, whereas HPV16 and 18 were observed predominantly in CIN III/CIS (p=0.01). No clear distribution pattern was observed for HPV31, 33, 52b and 58. Expression of HPV E6 and E7 transcripts was uniformly correlated with the different physical state of HPV DNA.

The complainant alleged that there was no scientific support to justify the claims that HPV types 6 and 11 had anything to do with cervical cancer. The complainant noted that 'histology CIN I' was now nearly accepted to have nothing to do with cervical cancer.

APPEAL BOARD RULING

The Appeal Board had some concerns that in the claim 'Benefit from 4 types - before and beyond cervical cancer', 'before … cervical cancer' related to time ie high-grade cervical dysplasia whereas 'beyond cervical cancer' related to anatomy ie vulval lesions or external genital warts. However the Appeal Board considered it unlikely that readers would assume that 'beyond' referred to a time after which a woman had developed cervical cancer given that the very prominent claim which preceded the claim at issue clearly referred to the prevention of cervical cancer.

The Appeal Board did not consider that the claim implied that HPV types 6, 11, 16 and 18 all caused cervical cancer as alleged.

Although noting its concern above, the Appeal Board considered that, in the context in which it appeared, the claim was not ambiguous or misleading and could be substantiated. No breach of Clauses 7.2 and 7.4 was ruled. The appeal was successful.

Complaint received 8 December 2006

Case completed 22 February 2007

PRINCIPAL HOSPITAL PHARMACIST v PLIVA PHARMA

Promotion of generic medicines

A principal hospital pharmacist complained about the promotion of generic medicines by representatives from Pliva Pharma.

The complaint referred to an email sent by a Pliva regional hospital manager to a colleague of the complainant which referred to the complainant's lack of response following a meeting about discounts.

The complainant stated that she had immediately switched the purchasing route on Cystistat the afternoon that she met with Pliva so that the trust was buying it at the cheapest possible price. However, many of the generic medicines discussed were in national contracts and there was an obligation to the trust to look at the prices offered elsewhere as Pliva's might not be the cheapest. The complainant had received one email and one telephone call asking what she had done and she duly informed both parties that she had not had time to sort through everything yet but she had not forgotten.

The Director decided that in relation to the allegations about the promotion of Cystistat there was no *prima facie* case to answer as the product was a device rather than a medicine and thus not subject to the Code.

The Panel noted that company representatives had met with the complainant to discuss, *inter alia*, the purchase price of Pliva's generic medicines. The complainant had received one email and one telephone call from Pliva asking what she had done and she duly informed the company that she had not had an opportunity to sort everything out. In addition to the complainant, Pliva had also been in contact with a nurse from the urology department regarding Cystistat. The email provided by the complainant was principally about Cystistat. It appeared that neither Pliva nor the nurse knew that the complainant had already organised its purchase. The Panel considered that Pliva had urged the nurse to contact the complainant about Cystistat, not about the generic medicines.

The Panel noted that the email was simply chasing an outcome to a meeting between Pliva representatives and the complainant. The Panel appreciated that the complainant may have been unhappy that the company had contacted a colleague. Nonetheless, the Panel did not consider that the conduct of the representatives or the content of the email were such as to disparage the complainant or query her professional integrity and no breach of the Code was ruled.

A principal hospital pharmacist complained about the promotion of generic medicines by representatives from Pliva Pharma Ltd.

COMPLAINT

An email sent by a Pliva regional hospital manager to a colleague of the complainant stated:

'I hope this message finds you in the best of health. Just a quick update to let you know that I came in to see … and … yesterday and went through what is happening.

Basically, myself and … [a senior manager] came to see [the complainant] about a month ago. At the end of this meeting it was agreed that we would put forward a scheme for [the complainant] to look at which included a discount on Cystistat and also the introduction of some new generic lines at a cost benefit to the trust. These measures were designed to assist the trust in achieving its goals of cost containment.

It has now been a few weeks and this matter has still has not been looked into. Please be assured that Pliva UK and most especially myself recognise the gravity of your situation and are willing to help in any way we can. There has to be though some impetus from the trust to engage in a dialogue in order to achieve a satisfactory settlement for all concerned.

Therefore could you please contact [the complainant] to see what's happening and whether she needs to contact us again before you have this meeting next week.'

To put things into context, the complainant stated that in relation to Cystistat, which Pliva originally came to see her about, she immediately switched the purchasing route on the afternoon that they saw her so that the trust was buying it at the cheapest possible prices. With regard to the other generic medicines, the complainant had pointed out that many of them were in national contracts and she was not keen to break the contracts. She also had an obligation to the trust to look at the prices offered by other generic manufacturers as Pliva's might not be the cheapest offer received.

The complainant had received one email and one telephone call asking what she had done and she duly informed both parties that she had not had time to sort through everything yet but she had not forgotten.

The complainant asked the Authority to look into the possibility of a breach of the Code.

When writing to Pliva, the Authority asked it to respond in relation to Clauses 8.2, 9.1 and 15.2 of the Code.

RESPONSE

Pliva submitted that Cystistat was not a medicine but a device and therefore not subject to the Code.

In relation to the generic medicines, Pliva stated that during a meeting between its representative, a senior manager and the complainant on 26 October, a significant overspend was described by the complainant on medicines within the trust. Pliva had as part of its product portfolio a range of generic medicines. On 30 October, a price offer was made on the output of this meeting on various medicines to the complainant. In an email message to the complainant, the senior manager stated:

'I have attached a pricing offer on our generics portfolio which is for … hospital only – this is positioned for you in the light of the overspend that you described to me in the hospital and its PFI status.'

He further added:

'If you do have any questions, please do not hesitate to contact me at any of the numbers below or by email. I have diarised to contact you in approximately 10 days time to determine if there is an opportunity on the other products that I have provided prices for.'

This was a price offer made in good faith complying with the general regular commercial practice of the industry. It was considered that further discussion would have been needed to complete any commercial outcome from this offer. Pliva supported the complainant's view that she had an obligation to the trust to look at prices offered by generic manufacturers and agreed that Pliva's might not be the cheapest offer.

Pliva denied a breach of Clauses 8.2, 9.1 or 15.2 of the Code.

Pliva provided a chronological list of all its dealings with the hospital with respect to this particular matter.

Pliva did not consider that its actions or the behaviour of its representatives had breached the Code and in particular it did not consider that there had been any breach of Clauses 8.2, 9.1 or 15.2. From its perspective, and what was clear from the chronology, this matter represented a simple lack of communication. The urology department at the hospital and clinical director did not seem to have been fully aware of Pliva's proposal regarding Cystistat and the fact that the complainant had implemented the change in purchasing route. The complaint was the first communication Pliva had received confirming that the purchasing route had been switched - reflecting the discussion that Pliva and the complainant had on 26 October. Pliva's representative was put under considerable pressure by the hospital to try and resolve a matter the urology department clearly considered of great importance. The communications sent both in content and timing, were made entirely in good faith in an attempt to try and resolve this matter. Pliva did not consider that its actions were anything other than a diligent attempt to meet customer needs. There was certainly no intention to disparage or otherwise make comment on any individuals involved.

PANEL RULING

Cystistat was a device rather than a medicine and was thus not subject to the Code. The Director thus decided that in relation to the allegations about the promotion of Cystistat there was no *prima facie* case to answer.

The Panel noted that company representatives had met with the complainant to discuss, *inter alia*, the purchase price of Pliva's generic medicines. The complainant had received one email and one telephone call from Pliva asking what she had done and she duly informed the company that she had not had an opportunity to sort everything out. In addition to the complainant, Pliva had also been in contact with a nurse from the urology department regarding the purchase of Cystistat. The email provided by the complainant was principally about Cystistat. It appeared that neither Pliva nor the urology nurse knew that the complainant had already organised its purchase. The Panel considered that Pliva had urged the nurse to contact the complainant about Cystistat, not about the generic medicines.

The Panel noted that the email was simply chasing an outcome to a meeting between Pliva representatives and the complainant. The Panel appreciated that the complainant may have been unhappy that the company had contacted a colleague. Companies had to ensure that they maintained high standards. Nonetheless, the Panel did not consider that the conduct of the representatives or the content of the email were such as to disparage the complainant or query her professional integrity; no breach of Clause 8.2 was ruled. The company and its representatives had not failed to maintain high standards; no breach of Clauses 9.1 and 15.2 was ruled.

Complaint received 7 December 2006

Case completed 16 February 2007

PRACTICE MANAGER v TEVA

Conduct of representative

A practice manager alleged that a representative of Teva had an extremely aggressive and demanding manner. The representative had arrived without an appointment and insisted on waiting for the complainant after telling the receptionist it was extremely important she saw her that day. The representative immediately launched into a clinical discussion and said it was very important that the practice changed its prescribing pattern regarding beclometasone. Teva marketed Qvar, a CFC-free beclometasone dipropionate (DBP) inhaler for asthma. The representative was very insistent on seeing a doctor or a nurse and wanted to have a private meeting that moment. When the representative was asked to leave literature she insisted she had to see them as it was very important for the practice. The complainant told the representative that the surgery got its prescribing advice from the primary care trust (PCT) but she would not accept this. The complainant alleged that the representative was scaremongering. When asked to comment on Teva's response, the complainant stated that the representative had implied that the practice should take her advice or its patients would suffer.

The Panel noted that both parties had accused the other of being curt. The complainant was very busy and the representative had to try to achieve her call objectives. The Panel did not know what asthma products the practice currently used. However it was likely that changes in the market place, particularly regarding the availability of DBP inhalers, would lead to changes for the practice.

Clearly it was of concern that the complainant had been annoyed by the representative's manner and that according to the complainant the impression given was that the practice would have to follow the representative's advice or patients would suffer. There appeared to have been something of a clash of personalities on the day. However it was not possible to determine where the truth lay. On the basis of the parties' submissions the Panel did not consider that there was sufficient evidence to show that on the balance of probabilities the representative had failed to maintain a high standard of ethical conduct. The Panel ruled no breach of the Code.

A practice manager complained about the conduct of a representative of Teva UK Limited. Teva marketed Qvar, a CFC-free beclometasone dipropionate (DBP) inhaler for asthma.

COMPLAINT

The complainant alleged that the representative's manner was extremely aggressive and demanding. The representative had arrived without an appointment and insisted on waiting for the complainant after telling the receptionist it was extremely important she saw her that day. The representative immediately launched into the clinical reasons and said it was very important that the practice changed its prescribing pattern regarding beclometasone. The representative was very insistent on seeing a doctor or a nurse and wanted to have a private meeting that moment. When the representative was asked if she would leave literature she insisted she had to see them as it was very important for the practice. The complainant told the representative that the surgery got its prescribing advice from the PCT but she would not accept this.

The complainant had been a practice manager for 7 years and had a lot of experience with representatives but had never come across one so aggressive and demanding. The complainant alleged that the representative was scaremongering and could have frightened a less experienced receptionist.

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

RESPONSE

Teva explained that the representative in question had called to see the complainant to introduce herself and discuss the changes currently happening that might affect patients under the care of the surgery eg guidance from the Medicines and Healthcare products Regulatory Agency (MHRA) to prescribe CFC-free BDP by brand and the announcement by GlaxoSmithKline that Becotide and Becloforte (both contained BDP) would be discontinued in 2007. The representative had previously discussed Qvar with the senior GP of the practice, who by the end of the conversation was in favour of Qvar.

When the representative entered the surgery she asked the receptionist if she could meet the practice manager as she had an important issue to discuss with her. The receptionist asked the practice manager if she would see the representative and then asked the representative to take a seat and wait. After a short period the practice manager saw the representative; her first question was 'What have you got to tell me that is so important?'

In response the representative explained about the MHRA guidance as well as GlaxoSmithKline discontinuing Becotide. The representative also tried to tell the complainant that she had already met the senior GP and that he expressed an interest in Qvar.

Before the representative could finish, the practice manager interrupted her and stated that this was a clinical matter, that it was up to the doctors and that it had nothing to do with her. The representative tried to explain why it was important for her to know about these issues as she would most probably be coordinating them, but she was interrupted again and asked if she was there to sell a medicine. The representative replied 'Yes as I am a sales representative selling Qvar' but also explained that she was there to let the complainant know about issues affecting the use of Qvar. The practice manager then told the representative that all this had nothing to do with her. The representative replied that she felt it was important for the complainant to know about it and explained the reasons why.

The representative submitted that the practice manager was direct and curt which made her feel uncomfortable. However, the representative considered that she had remained calm and professional during the conversation. The complainant did not tell the representative that she was unhappy, would complain to the company or bar her from the surgery. At the end of the conversation the representative courteously handed the complainant a diary which she accepted and thanked her for. The representative said goodbye and left the surgery.

Teva explained that its current code of conduct training for representatives included dedicated sessions within initial training courses, area meetings and national sales meetings. Every representative was issued with a copy of the Code and a copy of Code in the Field.

Each representative had signed to say that they had read and would abide by the Teva code of conduct which included complying with the ABPI Code.

In January, February and April 2006 Teva had run dedicated sessions on the ABPI Code at national sales meetings.

Teva submitted that on-going training continued for representatives on a 1:1 basis with the area sales manager. The representative in question had received six field visits, the last of which was on 15 November and at no time did she behave inappropriately or give the area sales manager cause for concern to think that she might do so. At all times the representative had behaved in a professional manner and had always remained within the Code. The area sales manager was surprised to receive this complaint as Teva had never received any complaint regarding the representative's conduct.

Teva submitted that on this occasion the discussions were important as they related to patient care. Recently it had been recognised that CFC-free BDP inhalers could be confused if prescribed generically and therefore the MHRA had recommended that all prescriptions for CFC-free BDP should be written by brand. Details were provided.

Teva agreed that any changes to prescribing habits within a surgery had to be requested by the physicians. However as the MHRA recommendation affected all CFC-free BDP prescribing it was usual practice to discuss the matter with the practice manager, as they must also be comfortable with the need to follow the recommendations. Usually this was well received and the importance was accepted. This was even more important in the current climate as GlaxoSmithKline had announced that it would discontinue its BDP medicines, Becotide and Becloforte, by September 2007.

The representative in question wished to discuss the above issues with the practice manager and Teva was very disappointed in the practice manager's response especially as she could have declined to see the representative at any time.

Teva submitted that this was an isolated incident in which there had been a misunderstanding between two individuals that had led to a customer feeling that Teva had not met its high levels of customer satisfaction and it took this very seriously. To this end, Teva would shortly conduct revision sessions for the representative on the Code and an additional training session to assess and review her selling skills; any deficiencies would be remedied.

Teva submitted that these steps would improve and increase its levels of compliance and ensure that it delivered customer services of a high standard to meet expectations.

In conclusion Teva submitted that it appeared that there was some misunderstanding but its representative behaved professionally in discussing issues that were important for patient care which included the MHRA's recommendations and GlaxoSmithKline's discontinuation of BDP products. This was an isolated incident and did not represent a breach of Clause 2 of the Code.

Teva did not accept that its representative was scaremongering because it knew that there was confusion in prescribing CFC-free inhalers and in this case it was very important that the products were prescribed by brand as Qvar should be prescribed at 50% of the dose of CFC-BDP and Clenil (HFA-BDP). Teva therefore submitted that this complaint did not represent a breach of Clauses 9.1 or 15.2 of the Code.

Teva submitted that it abided by both the letter and the spirit of the Code for all customer facing members of staff, to this end it invested a great deal in training and development to ensure that its representatives conducted themselves in the highest professional manner during all interactions with customers. Teva also recognised that the customer's perception was paramount and it prided itself in delivering first class customer service at all times.

Teva hoped that its actions would satisfy the complainant of its commitment to customer service and it would continue to take every effort to ensure that its staff behaved in a professional manner and complied with the Code.

FURTHER COMMENTS FROM THE COMPLAINANT

The complainant stated that she had no issue with a representative calling in to the practice without an appointment to leave information for the doctors, but she took issue with the manner in which the representative in question conducted herself. On arriving at the practice, the representative informed the receptionist that she had an important issue to discuss with the complainant. The receptionist thought that the representative was quite curt and her manner suggested that it was imperative for her to talk to the complainant there and then.

The representative immediately launched into a clinical explanation of her medicine to which the complainant had to stop her because she was not clinical or in a position to make any decisions regarding the prescribing policy of the GPs. The representative then wanted to discuss the matter further in a meeting room which the complainant considered inappropriate for the reasons stated above. The complainant was very busy and this was an unplanned meeting for which she did not have the time.

The complainant was sure the representative was very enthusiastic and knowledgeable about her medicine and was anxious to inform the doctors about it but her manner was not appropriate. The complainant considered that the representative had taken the attitude that the practice had to take her advice or its patients would suffer.

The complainant noted that the practice was visited by a number of representatives to give information about their products but advice regarding changes of medicines was given to the practice by the local primary care trust and the information it got from representatives was 'interesting' rather than 'important'.

The complainant stated that she had seen many representatives over the last seven years as a practice manager and this was the first time she had encountered this type of behaviour. Perhaps an acknowledgement that the representative's manner was inappropriate and further customer training would resolve this issue.

PANEL RULING

The Panel noted that the parties' accounts differed; it was difficult in such cases to know exactly what had transpired. 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 actually submit a complaint.

Both parties had accused the other of being curt. The complainant was very busy and the representative had to try to achieve her call objectives. The Panel did not know what if any CFC-free products the practice currently used. However it was likely that the prescribing of CFC-free BDP would lead to changes for the practice. The MHRA had issued guidance on the matter, GlaxoSmithKline had announced the withdrawal in 2007 of Becotide and Becloforte, the dosing of the two CFC-free BDP products were different and the senior GP at the practice had, according to the representative, expressed an interest in Qvar.

Clearly it was of concern that the complainant had been annoyed by the representative's manner and that according to the complainant the impression given was that the practice would have to follow the representative's advice or patients would suffer. There appeared to have been something of a clash of personalities on the day. However it was not possible to determine where the truth lay. On the basis of the parties' submissions the Panel did not consider that there was sufficient evidence to show that on the balance of probabilities the representative had failed to maintain a high standard of ethical conduct. The Panel ruled no breach of Clauses 15.2 and 9.1. It thus followed that there was no breach of Clause 2.

Complaint received 11 December 2006

Case completed 2 March 2007

PRIMARY CARE TRUST PRESCRIBING ADVISOR v ROCHE and GLAXOSMITHKLINE

Bonviva leavepiece

A primary care trust prescribing advisor complained about a Bonviva (ibandronic acid) leavepiece issued jointly by Roche and GlaxoSmithKline. Bonviva 150mg (one tablet) once a month was indicated for the treatment of osteoporosis in postmenopausal women at increased risk of fracture.

A page of the leavepiece headed 'Efficacy' featured a box headed 'Bonviva: reduction in risk of vertebral fracture over 3 years'. A large downward arrow with 62% on it appeared to the left of a statement 'Data adapted from a randomised, double-blind, placebo-controlled, three-year study, involving postmenopausal women, of whom 977 received Bonviva 2.5mg daily, and 975 received placebo' referenced to Chesnut *et al* 2004.

The complainant noted that the study cited did not use once-monthly Bonviva and alleged that it was unacceptable and unethical to use data from a daily formulation to promote a monthly formulation of the same medicine. The vertebral fracture efficacy of once-monthly Bonviva had not been demonstrated in clinical trials, therefore the promotional material was very misleading.

The Panel noted Roche and GlaxoSmithKline's comments about the regulatory guidance for the use of bridging studies when applying for a marketing authorization for medicines that had already demonstrated anti-fracture efficacy for a specific dose. From the Bonviva 150mg summary of product characteristics (SPC) it was clear that Bonviva once-monthly reduced the risk of vertebral fractures.

The Panel noted that every page of the leavepiece, except the one at issue, referred specifically to Bonviva once-monthly. The page at issue referred only to Bonviva. In the Panel's view most readers would not note this difference and assume that everything in the leavepiece was about Bonviva once-monthly which was not so. The claim that there was a 62% reduction in the risk of vertebral fractures over 3 years related to data for patients on once-daily Bonviva. There was no direct clinical data to support a 62% reduction in the risk of vertebral fractures for patients on Bonviva once-monthly. Although a qualification was included next to the risk reduction claim, the Panel considered that in the context of the leaflet as a whole it was not sufficiently clear that the 62% risk reduction claim applied to the once-daily dose. The leaflet was misleading in this regard and a breach of the Code was ruled.

Upon appeal, the Appeal Board noted that the SPC referred to a study looking at bone mineral density (BMD) which had concluded that Bonviva 150mg once monthly was at least as effective as Bonviva 2.5mg daily at increasing BMD in a two year study. The Bonviva 150mg SPC also stated that based on those results Bonviva 150mg once monthly was expected to be at least as effective in preventing fractures as Bonviva 2.5mg daily. In addition the SPC included details of a study in which Bonviva 2.5mg daily had been shown to reduce the relative risk of fracture by 62% over 3 years. It was by bridging data from one formulation to another in this way that Bonviva 150mg once monthly had obtained its marketing authorization. The Appeal Board considered it acceptable to use such data in promotional material for Bonviva 150mg but noted that care should be taken to ensure that it was made clear that the source data was from the 2.5mg daily dose. In the Appeal Board's view the page in question did make it sufficiently clear that the data was adapted from a study on 2.5mg Bonviva daily. No breach of the Code was ruled.

A prescribing advisor to a primary care trust (PCT) complained about a leavepiece (ref P117551) for Bonviva (ibandronic acid). Bonviva was co-promoted by Roche Products Limited and GlaxoSmithKline UK Ltd and the matter was taken up with both companies. According to its summary of product characteristics (SPC) Bonviva 150mg was indicated for the 'treatment of osteoporosis in postmenopausal women at increased risk of fracture (see Section 5.1). A reduction in the risk of vertebral fractures has been demonstrated, efficacy on femoral neck fractures has not been established'. The recommended dose was one tablet (150mg) once a month.

Page three of the leavepiece was headed 'Efficacy' followed by 'Bonviva offers proven vertebral fracture efficacy'. Underneath this was a box headed 'Bonviva: reduction in risk of vertebral fracture over 3 years', a large downward arrow with 62% on it appeared to the left of a statement 'Data adapted from a randomised, double-blind, placebo-controlled, three-year study, involving postmenopausal women, of whom 977 received Bonviva 2.5mg daily, and 975 received placebo' referenced to Chesnut *et al* (2004).

COMPLAINT

The complainant stated that the data quoted was from the BONE study which did not use once-monthly Bonviva. The complainant alleged that it was unacceptable and unethical to use data from a daily formulation to promote a monthly formulation of the same medicine. The vertebral fracture efficacy of once-monthly Bonviva had not been demonstrated in

clinical trials, therefore the promotional material was very misleading.

When writing to the companies, the Authority asked them to respond in relation to Clause 7.2 of the Code.

RESPONSE

The companies disagreed that the leavepiece was misleading and therefore denied a breach of Clause 7.2 of the Code.

Currently there were three licensed formulations of Bonviva: Bonviva 2.5mg tablets (daily) (this formulation was not marketed or promoted in the UK); Bonviva 150mg tablets (monthly) and Bonviva 3mg/3ml solution for intravenous injection (every 3 months).

The indication for Bonviva 150mg tablets, as described in the SPC was 'Treatment of osteoporosis in postmenopausal women at increased risk of fracture (see Section 5.1). **A reduction in the risk of vertebral fractures has been demonstrated**, efficacy on femoral neck fractures has not been established' (emphasis added).

Therefore, from a regulatory perspective, the vertebral fracture efficacy of once-monthly Bonviva had been demonstrated (the indication being issued as part of the marketing authorization). For Bonviva 150mg (monthly formulation) the licensed indication relating to vertebral fracture reduction was, at least in part, based on data from clinical trials for the daily formulation. This extrapolation of clinical data from the daily to the monthly formulation, otherwise known as 'bridging', was fully accepted in the therapy area of osteoporosis by regulatory authorities and was widely accepted in medical practice largely as a result of ethical considerations in clinical research.

Bridging concept

In osteoporosis, regulatory authorities had recognised that it was unethical to perform additional, large, placebo-controlled studies to assess anti-fracture efficacy for compounds that had already demonstrated anti-fracture efficacy and been granted the indication of 'Treatment of osteoporosis in postmenopausal women at high risk of fracture' in relation to a new dose, formulation or route of administration. This concept was part of the European Medicines Evaluation Agency's (EMEA's) Guideline on the Evaluation of Medical Products in the Treatment of Primary Osteoporosis (CPMP/EWP/552/95, 2006) which stated (paragraph 5.3.3):

> 'Alternative surrogate endpoints like biochemical markers of bone turnover should be used in bridging studies after a thorough analysis of historical studies showing a good correlation between pharmacokinetic exposures, the pharmacodynamic response and the reduction in fracture risk. **To avoid having to conduct separate fracture studies, the time-course of changes in surrogate markers should recapitulate the time-course observed for the original dosing regimen. This should apply to any surrogate endpoint that is known to be associated with fracture risk, such as BMD and/or a biochemical marker.'**(emphasis added)
>
> 'Equivalence or non-inferiority can be tested in a bridging study...'

In line with guidance from the EMEA, data from the 2.5mg daily formulation of Bonviva was 'bridged' in order to obtain the marketing authorization for the 150mg monthly formulation.

Presenting the vertebral fracture data for the daily dose of Bonviva ensured that the leavepiece was 'sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine' and that the reader was clear on the origin of the data and the claims associated with it.

The text directly adjacent to the downward arrow on page three of the leavepiece clearly stated that the vertebral efficacy data was derived from a study in which patients received Bonviva 2.5mg daily or placebo. This was presented in an accurate, balanced, fair, objective and unambiguous manner. The way in which the data was presented was not misleading.

Summary

i) The vertebral fracture efficacy of once-monthly Bonviva had been demonstrated (based on the bridging concept) and was reflected in the wording of the licensed indication as described in the SPC;
ii) in osteoporosis it was acceptable and ethical to use fracture efficacy data from a daily formulation to promote a monthly formulation of the same medicine as long as it was made clear from which dose and formulation the clinical data was derived;
iii) the bridging concept in osteoporosis was acknowledged and accepted by regulatory agencies and medical practice and allowed the extrapolation of fracture data, in this case, from a daily to a monthly formulation of the same compound;
iv) it was clearly stated in the leavepiece that the data supporting the vertebral fracture efficacy claims was from patients who received Bonviva 2.5mg daily (this was also clearly described by the complainant).

In conclusion, for the reasons detailed above, the companies submitted that the leavepiece was accurate, balanced, fair, objective and unambiguous and based on an up-to-date evaluation of all the evidence and reflected the evidence clearly. It did not mislead either directly or by implication, by distortion, exaggeration or undue emphasis. Additionally, the material was sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine and was therefore not in breach of Clause 7.2 of the Code.

PANEL RULING

The Panel noted Roche and GlaxoSmithKline's comments about the regulatory guidance for the use of bridging studies when applying for a marketing authorization for medicines that had already demonstrated anti-fracture efficacy for a specific dose. From the Bonviva 150mg SPC it was clear that Bonviva once-monthly reduced the risk of vertebral fractures.

The Panel noted that every page of the leavepiece, except the one at issue, referred specifically to Bonviva once-monthly. The page at issue, page three, referred only to Bonviva. In the Panel's view most readers would not note this difference and assume that everything in the leavepiece was about Bonviva once-monthly which was not so. The claim that there was a 62% reduction in the risk of vertebral fractures over 3 years related to data for patients on once-daily Bonviva. There was no direct clinical data to support a 62% reduction in the risk of vertebral fractures for patients on Bonviva once-monthly. Although a qualification was included next to the risk reduction claim, the Panel considered that in the context of the leaflet as a whole it was not sufficiently clear that the 62% risk reduction claim applied to the once-daily dose. The leaflet was misleading in this regard and a breach of Clause 7.2 was ruled.

APPEAL BY ROCHE AND GLAXOSMITHKLINE

The companies stated that the basis for appeal was twofold; firstly that the leavepiece was sufficiently clear as to the source of the 62% fracture reduction data and could not be considered misleading under Clause 7.2 and secondly, although the leavepiece had been withdrawn some time ago, and subsequent materials developed, it was not clear from the Panel's ruling what changes would be needed to ensure that no breach of undertaking could be ruled in future.

From the Panel's ruling and a telephone discussion with the Authority the companies submitted that the foundation for the ruling related to the manner in which the data was presented and not with the actual use of it which was the initial allegation in the complaint.

The companies understood that the Panel accepted that the use of the 62% vertebral fracture data from the initial 2.5mg daily Bonviva preparation in the promotion of Bonviva was valid and not misleading per se. The Panel considered however that a health professional would not be expected to read a leavepiece in any great depth and thus as the leavepiece promoted the licensed and marketed dose of Bonviva 150mg the source of the 62% vertebral fracture data needed to be clearer than in a detail aid for example, which would be accompanied by verbal messaging. The companies did not accept this and submitted that to assume so did not recognise the professional standing of the reader.

The companies submitted that the Panel had considered that the repeated reference to the 150mg dose throughout the leavepiece meant that the qualification next to the arrow displaying the percentage fracture reduction was not sufficient to allow the health professional to make a balanced determination of the value of Bonviva in the management of postmenopausal women. This was considered, by the Panel, to be especially pertinent given that the information was contained in a leavepiece which the reader would not be expected to read in any great depth. The companies submitted that the qualification within the leavepiece was unambiguous, based on up-to-date data, which was also included in the Bonviva 150mg SPC. The data were presented clearly and were not inconsistent with the SPC and were the basis for efficacy upon which the licence was granted; so this, in no way, misled the reader.

The companies submitted that the dosage used in the study, 2.5mg daily, was positioned directly next to the arrow within the same box and was in a font similar to the other bullet points in the leavepiece. The companies had not used an asterix and placed the qualification away from the arrow in a smaller text.

The companies submitted that if the 2.5mg dose was given the same prominence as the 150mg dose within the leavepiece, in terms of placement and font size, this could confuse health professionals as to what to prescribe. The only available oral dose of Bonviva was 150mg monthly.

The companies submitted that whilst it appeared that the Panel had accepted that the use of bridging data across doses was acceptable in promotional material, if this finding of a breach were to be upheld it would have wide reaching consequences on how bridging data was presented across many different disease and therapy areas and potentially confuse health professionals as to the doses available to prescribe. There had to be a balance between being clear as to the source of the original efficacy data and not over-emphasising doses or preparations that were not actually available irrespective of whether the presentation of the data was a leavepiece, detail aid or advertisement.

The companies submitted that there seemed to be a possible misunderstanding about the relevance of bridging data. It was fundamentally wrong to imply that because fracture data was available for the 2.5mg dose and not for the 150mg dose that this suggested inferiority of the latter. Bonviva 150mg was indicated for prevention of vertebral fracture. The indication in the SPC was not qualified by any statement regarding the dose used to obtain that indication. Clause 3.2 stated that promotion of a medicine, *inter alia*, must not be inconsistent with the particulars listed in its SPC.
A ruling that implied that claims about fracture reduction must always be accompanied by a statement that this was based only on data for 2.5mg was not consistent with the marketing authorization and indeed undermined the legitimacy of that marketing authorization when the same data was used as a basis for that approval.

The complainant's initial concern was not that it was not sufficiently clear that the source of the 62% vertebral fracture data was from a trial carried out with 2.5mg daily Bonviva, rather that it was used at all. Indeed it was sufficiently clear to the complainant that the data was from the 2.5mg daily dose as opposed to the 150mg dose for her to conclude that, it was unethical to use daily data when promoting a monthly dose.

The companies noted that in its ruling the Panel stated that given the context of the material it considered that the leavepiece was not sufficiently clear that the 62% risk reduction claim applied to the daily dose. As previously stated, one of the reasons that the companies had appealed was that it was unclear what 'sufficiently clear' meant in this context and thus it was not clear from the Panel's ruling what changes would be needed to ensure that no breach of undertaking could be ruled in future. Any finding would be equally attributable irrespective of the type of material in which these data were presented and thus to determine what was likely and not likely to be read for each type of material was not evident from the correspondence received.

In summary the companies submitted that the leavepiece was not misleading in its presentation of the vertebral fracture data on the following points and was therefore not in breach of Clause 7.2:

- Therapeutic equivalence had been demonstrated by the use of the accepted practice of bridging data between the daily and monthly dose of Bonviva.
- The data presented was consistent with data presented in the Bonviva 150mg SPC
- The qualification relating to the vertebral fracture data claim was directly next to the percentage arrow, was in the same size font as the other bullet points within the leavepiece and was complete in its explanation.
- To further emphasise the 2.5mg dose, which was unavailable in the UK could mislead health professionals as to the oral doses available and therefore impact on patient care. It could also be considered inconsistent with the prescribing information used on Bonviva materials and thus open to challenge.
- A leavepiece was not designed to be skim read and to assume so was incorrect. The clarity as to the source of the data was sufficiently clear in the leavepiece and sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine.

COMMENTS FROM THE COMPLAINANT

The complainant made no further comment regarding the use of bridging data.

APPEAL BOARD RULING

The Appeal Board noted that the SPC referred to a study looking at bone mineral density (BMD) which had concluded that Bonviva 150mg once monthly was at least as effective as Bonviva 2.5mg daily at increasing BMD in a two year study. The Bonviva 150mg SPC also stated that based on those results Bonviva 150mg once monthly was expected to be at least as effective in preventing fractures as Bonviva 2.5mg daily. In addition the SPC included details of a study in which Bonviva 2.5mg daily had been shown to reduce the relative risk of fracture by 62% over 3 years. It was by bridging data from one formulation to another in this way that Bonviva 150mg once monthly had obtained its marketing authorization. The Appeal Board considered it acceptable to use such data in promotional material for Bonviva 150mg but noted that care should be taken to ensure that it was made clear that the source data was from the 2.5mg daily dose. In the Appeal Board's view the page in question did make it sufficiently clear that the data was adapted from a study on 2.5mg Bonviva daily. No breach of Clause 7.2 was ruled. The appeal was successful.

Complaint received 18 December 2006

Case completed 22 February 2007

PRIMARY CARE TRUST ASSISTANT DIRECTOR OF CLINICAL SERVICES v TRINITY-CHIESI

Primary Care Report – CFC-free inhalers

The assistant director of clinical services at a primary care trust (PCT) complained about special edition 3, December 2006, of Primary Care Report which dealt with CFC-free inhalers. At the bottom of the front cover it was stated that 'This edition of *Primary Care Report* is sponsored by Trinity-Chiesi Pharmaceuticals Ltd'.

The item comprised four pages. The front page was headed 'Becotide/Becloforte withdrawal forces treatment reviews' and referred to the transition to CFC-free beclometasone dipropionate (BDP). Trinity-Chiesi's BDP product, Clenil Modulite, was described as a CFC-free, dose equivalent alternative to Becotide/Becloforte.

The complainant stated that this document purported to be 'The first choice for primary care leaders' and appeared to be a series of articles regarding inhaled steroid prescribing. On reading the articles the complainant considered them to be one long advertisement for Clenil Modulite. It was extremely one sided and contained technical inaccuracies that further pushed the prescribing of this preparation.

The first article, on Becotide withdrawal, stated that Department of Health (DoH) policy was that 'CFCs will no longer be considered essential in products containing inhaled steroids in the UK once two alternative products containing beclometasone are available'. This was not referenced but was different to the advice that was being given from the local strategic health authority prescribing advisor who stated that there must be two preparations of equal potency available.

This was not the case currently and until this happened generic BDP would continue to be available. This was not mentioned in the article neither was it stated that when beclometasone (sic) was discontinued patients could be simply switched to the generic equivalent which was considerably cheaper then Clenil. The second article gave an example of a switch programme from Becotide to Clenil. The advertisement continued. The third article was a review of Clenil. The advertisement continued.

The complainant considered it unacceptable to dress up an advertisement for a medicine as a series of articles. The Primary Care Report stated that it was sponsored by Trinity-Chiesi; however this did not protect the reader from the bias that was inherent in the articles which the complainant considered were misleading and incorrect.

The Panel noted that the Primary Care Report had been sponsored by Trinity-Chiesi and approved by the company as a piece of promotional material.

The Panel considered the immediate visual impression of the front page. Given the recent changing nature of the Primary Care Report, the Panel considered that it would be difficult to substantiate the statement beneath the title Primary Care Report that it was 'The first choice for primary care leaders'. The left hand column described Clenil Modulite as a CFC-free dose equivalent alternative to Becotide/Becloforte. As well as including the declaration of sponsorship, the front page stated that prescribing information was available on page 4. The main article on page 1 gave no details as to the status of the author. The article on page 2 was written by a freelance journalist. Although the Primary Care Report was dated and had an edition number, suggesting one in a series of publications, the Panel considered that on balance most readers would view the material as promotional. The document did not look like a medical journal or any other official publication. The Panel did not consider that the promotional nature of the material had been disguised. No breach of the Code was ruled.

The Panel noted the 1999 DoH Transition Strategy stated that the use of CFCs in a medicine containing beclometasone would no longer be considered essential once two alternative CFC-free MDI products containing the same medicine and meeting the needs of all patient groups were available from two different producers. In addition the transition strategy stated that CFCs in inhaled steroids would no longer be considered essential once two alternative products containing beclometasone and at least one CFC-free MDI product for each of budesonide and flucticasone were available in an adequate range of doses. This was included in the Primary Care Report article.

The Panel noted that the statement about the DoH advice was not referenced but the Code did not require it to be so. The Code required that all claims etc were capable of substantiation. The Panel noted there appeared to be a discrepancy between the DoH advice and the advice given by the complainant's strategic health authority. The Primary Care Report was not misleading in this regard and no breach of the Code was ruled.

The assistant director of clinical services at a primary care trust (PCT) complained about special edition 3, December 2006, of Primary Care Report which dealt with CFC-free inhalers. At the bottom of the front

cover it was stated that 'This edition of *Primary Care Report* is sponsored by Trinity-Chiesi Pharmaceuticals Ltd'.

The item comprised four pages. The front page was headed 'Becotide/Becloforte withdrawal forces treatment reviews' and referred to the transition to CFC-free beclometasone dipropionate (BDP). Trinity-Chiesi's BDP product, Clenil Modulite, was described as a CFC-free, dose equivalent alternative to Becotide/Becloforte.

COMPLAINT

The complainant stated that this document purported to be 'The first choice for primary care leaders' and appeared to be a series of articles regarding inhaled steroid prescribing. On reading the articles the complainant considered them to be one long advertisement for Clenil Modulite. It was extremely one sided and contained technical inaccuracies that further pushed the prescribing of this preparation.

The first article, on Becotide withdrawal, stated that Department of Health (DoH) policy was that 'CFCs will no longer be considered essential in products containing inhaled steroids in the UK once two alternative products containing beclometasone are available'. This was not referenced but was different to the advice that was being given from the local strategic health authority prescribing advisor who stated that there must be two preparations of equal potency available.

This was not the case currently and until this happened generic BDP would continue to be available. This was not mentioned in the article neither was it stated that when beclometasone (sic) was discontinued patients could be simply switched to the generic equivalent which was considerably cheaper then Clenil. The second article gave an example of a switch programme from Becotide to Clenil. The advertisement continued. The third article was a review of Clenil. The advertisement continued.

The complainant did not consider that it was acceptable to dress up an advertisement for a medicine as a series of articles. The Primary Care Report stated that it was sponsored by Trinity-Chiesi; however this did not protect the reader from the bias that was inherent in the articles. The complainant considered that these articles were misleading and incorrect.

When writing to Trinity-Chiesi, the Authority asked it to respond in relation to Clauses 7.2, 9.1 and 10.1 of the Code.

RESPONSE

Trinity-Chiesi stated that Primary Care Report was published by a long-established publisher of medical journals and titles. Primary Care Report began as a weekly publication in 2002 and targeted 12,500 primary care decision-makers in England. However, in response to the changing NHS environment and the needs and dynamics of PCTs, the publishers stopped regular publication of Primary Care Report in 2005 and re-launched the title as a sponsored supplement in early 2006. The sponsored supplement had always carried the same statement 'first choice for primary care leaders' since it was launched. This publication operated as a sole sponsored journal with key opinion leader interviews and articles and a back page for the sponsor's product or corporate advertisement.

Trinity-Chiesi sponsored the December 2006 edition of Primary Care Report, which was sent to 28,000 GPs as a supplement to the BMJ (which also evaluated the copy to ensure it did not infringe its publishing ethos), sent to approximately 11,200 primary care organisation contacts across England (including public health, finance, medicines management and commissioning representatives) and distributed via the Trinity-Chiesi sales team (17,500 printed).

Whilst Trinity-Chiesi was sorry that the complainant appeared to have been disappointed with the content the company believed it was clearly a promotional piece. It was a stand alone booklet which stated on the front cover that it had been sponsored by a pharmaceutical company; this statement was made prominent by a highlighted band and in addition the text was larger than the body copy. The document also contained a number of other indications that it was a promotional item eg it contained prescribing information and clearly stated where this could found, and the most prominent mention of the product name carried a large inverted black triangle. This supplement was not one sided and focused on the two alterative CFC-free BDP pressurised inhalers that were currently available. Trinity-Chiesi did not believe it could be considered to be disguised promotion (Clause 10.1).

Trinity-Chiesi noted that the DoH document 'UK Transition Strategy for CFC-based MDIs [metered dose inhalers] – September 1999' stated that CFCs would no longer be considered essential in products containing inhaled steroids in the UK once two or more alternative products containing beclometasone and at least one CFC-free MDI for each of budesonide and fluticasone were available in an adequate range of doses for all patient groups. There were no published updates to this document and Trinity-Chiesi believed that it represented current policy. The Code did not require every item of information to be referenced although all statements made must be capable of substantiation as the advice given in the article at issue thus was. Clearly there appeared to be a discrepancy between the UK Transition Strategy document and the advice given (or interpretations of advice given) by the complainant's strategic health authority. Trinity-Chiesi did not believe that the advice was in breach of Clause 7.2 of the Code; it was an accurate and unambiguous reflection of current DoH policy.

The Primary Care Report aimed to highlight the withdrawal of two major CFC-containing inhaled steroids, GlaxoSmithKline's Becotide and Becloforte, within the context of the DoH policy on CFC-free MDIs and the availability of Clenil Modulite. It discussed the

pragmatic solutions and processes that the quoted health professionals had identified as being appropriate to implement once they had decided that their patients would need to change to a CFC-free inhaler. The Primary Care Report did not state that patients on Becotide or Becloforte **would** have to change to a CFC-free inhaler, only that in view of the eventual need to change all patients to CFC-free devices, and the recent availability of a CFC-free BDP which enabled a direct switch, it might be appropriate to change patients directly to Clenil Modulite. Trinity-Chiesi believed that this argument was not misleading and had been presented in a balanced and accurate manner. Trinity-Chiesi did not believe that there was a breach of Clause 7.2.

Trinity-Chiesi regretted causing offence to any customer; it had not received any other complaints or negative comments about the item which was reviewed and approved through the company's Code compliance process. Trinity-Chiesi believed that the issue of CFCs was particularly important given current environmental concerns and that highlighting the effects of the eventual withdrawal of CFC-containing inhalers on those working in primary care was a responsible action, as well as being in line with its promotional strategy. In producing this item Trinity-Chiesi believed that it had upheld the high standards required.

PANEL RULING

The Panel noted that it was acceptable for companies to sponsor material. It had previously been decided 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 interests. It was possible for a company to sponsor material which mentioned its own products and not be liable under the Code for its content, but only if it had been a strictly arm's length arrangement with no input by the company and no use by the company of the material for promotional purposes.

The Panel noted that the Primary Care Report had been sponsored by Trinity-Chiesi and used by its representatives. No information had been given about the role of Trinity-Chiesi in the production of the Primary Care Report. The company had approved the item as a piece of promotional material.

The Panel considered the immediate visual impression of the front page. Given the changing nature of the Primary Care Report, the Panel considered that it would be difficult to substantiate the statement that it was 'The first choice for primary care leaders'. The left hand column described Clenil Modulite as a CFC-free dose equivalent alternative to Becotide/Becloforte. As well as including the declaration of sponsorship, the front page stated that prescribing information was available on page 4. The main article on page 1 gave no details as to the status of the author. The article on page 2 was written by a freelance journalist. Although the Primary Care Report was dated and had an edition number, suggesting one in a series of publications, the Panel considered that on balance most readers would view the material as promotional. The document did not look like a medical journal or any other official publication. The Panel did not consider that the promotional nature of the material had been disguised. No breach of Clause 10.1 was ruled.

The Panel noted the 1999 DoH Transition Strategy stated that the use of CFCs in a medicine containing beclometasone would no longer be considered essential once two alternative CFC-free MDI products containing the same medicine and meeting the needs of all patient groups were available from two different producers. In addition the transition strategy stated that CFCs in inhaled steroids would no longer be considered essential once two alternative products containing beclometasone and at least one CFC-free MDI product for each of budesonide and fluticasone were available in an adequate range of doses. This was included in the Primary Care Report article.

The Panel noted that the statement about the DoH advice was not referenced but under the Code it was not required to be so. The Code required that all claims etc were capable of substantiation. The Panel noted there appeared to be a discrepancy between the DoH advice and the advice given by the complainant's strategic health authority. The Primary Care Report was not misleading in this regard and no breach of Clause 7.2 was ruled.

The Panel noted its no breach rulings above and thus decided there was no breach of Clause 9.1.

Complaint received 19 December 2006

Case completed 20 February 2007

CASE AUTH/1936/12/06

PARAGRAPH 17/DIRECTOR V SCHERING HEALTH CARE

Advertisement to the public and a website

During the consideration of Case AUTH/1921/11/06 the Panel was concerned about an advertisement feature issued by Schering Health Care and published in the Marks & Spencer magazine, Christmas 2006. The advertisement was headed 'Time for you to take control' and was about long acting reversible contraception (LARC). A highlighted box of text described various LARC methods available. The first was the intrauterine system (IUS), which readers were told released 'progestogen where needed, so you only absorb a low dose of hormones' and was even more reliable than the pill. Comparable data, where appropriate, was not given for any of the other LARC methods referred to (implant, injection and intrauterine device (IUD)). The Panel was concerned that by giving more positive data about the IUS than the other methods the material was not balanced and some women might be encouraged to ask their doctor or other health professional to prescribe that method. The Panel noted that Schering Health Care marketed, Mirena (levonorgestrel), the only IUS available in the UK.

The Panel was further concerned about the content of the Schering Health Care website www.modernmotherhood.co.uk referred to in the advertisement. The home page featured a box 'The GP is in!' which linked readers to frequently asked questions about LARC and to the real life experiences of five mums. Each of the women profiled had been successfully prescribed an IUS. There were no profiles of women using any other method of LARC. The Panel was concerned that the website was not balanced and that its content would encourage readers to ask their doctor or other health professional to prescribe Mirena.

The Panel decided to take the matter up with Schering Health Care as a complaint (Case AUTH/1936/12/06) under Paragraph 17 of the Constitution and Procedure.

The Panel noted that the descriptions of the different LARC methods in the advertisement did not use the same parameters. The reliability of the IUS was compared with that of the pill when no equivalent data was given for the IUD, implant or injection. Similarly the progestogen level of the IUS was described as low whereas no description was given for the progestogen level in the implant or injection. The Panel considered that the content of the highlighted box would encourage women to ask for an IUS which, in effect, would be a request for Mirena. A breach of the Code was ruled.

The Panel considered that as the case studies on the website only related to women using the IUS that section was not balanced. Schering Health Care should have ensured that each type of LARC was represented by case studies. The material would encourage women to ask for the IUS which in effect would be a request for Mirena. The Panel ruled a breach of the Code.

COMPLAINT

During the consideration of Case AUTH/1921/11/06 the Panel was concerned about an advertisement feature issued by Schering Health Care Ltd and published in the Marks & Spencer magazine, Christmas 2006. The advertisement was headed 'Time for you to take control' and was about long acting reversible contraception (LARC). A highlighted box of text gave details of various LARC methods available. The first method described was the intrauterine system (IUS), which readers were told released 'progestogen where needed, so you only absorb a low dose of hormones' and was even more reliable than the pill. Comparable data regarding progestogen absorption was not given for implants or injection and the comparative efficacy data versus the pill was not given for any of the other LARC methods (implant, injection and intrauterine device (IUD)). The Panel was concerned that by giving more positive data about the IUS than the other methods the material was not balanced and some women might be encouraged to ask their doctor or other health professional to prescribe that method. The Panel noted that Schering Health Care marketed an IUS, Mirena (levonorgestrel).

The Panel was further concerned about the content of the Schering Health Care website www.modernmotherhood.co.uk referred to in the advertisement. The home page featured a box 'The GP is in!' which linked readers to frequently asked questions about LARC and to the real life experiences of five mums. Each of the women profiled had been successfully prescribed an IUS. There were no profiles of women using any other method of LARC. The Panel was concerned that the website was not balanced and that its content would encourage readers to ask their doctor or other health professional to prescribe Mirena.

The Panel decided to take the matter up with Schering Health Care as a complaint (Case AUTH/1936/12/06) under Paragraph 17 of the Constitution and Procedure.

When writing to Schering Health Care the Authority asked the company to respond in relation to the requirements of Clauses 2, 9.1 and 20.2 of the Code.

RESPONSE

Schering Health Care submitted that the highlighted box of text gave details of the various LARC methods available together with a short description. The first method described was the IUS which readers were told released 'progestogen where needed, so you only absorb a low dose of hormones'. Readers were also told that the IUS was even more reliable that the pill. The fact that the IUS was situated within the uterus and released progestogen to the surrounding tissue where it had the majority of its effects was unique to that method (Mirena summary of product characteristics (SPC), French and Guillebaud 2003). It had not seemed relevant or appropriate to mention absorption of progestogen for other methods. Furthermore, although comparative efficacy data versus the pill was not given for any of the other LARC methods, other equally relevant positive aspects were highlighted for these methods. For example readers were told that the IUD was not affected by other medicines and that the implant could be used by women of any age. Therefore, positive data were indeed highlighted for the other LARC methods. Schering Health Care submitted that the material was balanced and women would not be encouraged to ask their doctor or other health professional for the IUS over and above any of the other LARC methods.

Schering Health Care submitted that with respect to the **www.modernmotherhood.co.uk** website, there were five case histories of mums who had been successfully prescribed the IUS. A facility was provided for women to write in with their own stories which would then be considered for inclusion on the site. However, no case histories were submitted. Therefore, unfortunately, although the rest of the website was of a high standard, balanced, fair and accurate, the lack of provision of additional case histories had left this section of the website only describing women who had been successfully prescribed the IUS. On the assumption that Schering Health Care did not anticipate receiving case studies from women as expected, this section of the website was removed.

Schering Health Care confirmed that Mirena was the only IUS available in the UK.

Schering Health Care submitted that in view of the above the 'Time for you to take control' advertisement satisfied the requirements of Clauses 2, 9.1 and 20.2 respectively as a non-promotional health information piece that was of a high standard, balanced, fair and accurate.

PANEL RULING

The Panel noted that in accordance with Clause 20.2 of the Code companies could make available information about prescription only medicines to the public either directly or indirectly. Such information must be factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. Further, statements must not be made for the purpose of encouraging members of the public to ask their health professional to prescribe a specific prescription only medicine. Particular care was needed when referring to types of medicine when there was only one medicine that met the description. In this regard the Panel noted that Mirena was the only IUS available in the UK.

The Panel noted that the descriptions of the different LARC methods in the advertisement did not use the same parameters. The reliability of the IUS was compared with that of the pill when no equivalent data was given for the IUD, implant or injection. Similarly the progestogen level of the IUS was described as low whereas no description was given for the progestogen level in the implant or injection. The Panel considered that the content of the highlighted box would encourage women to ask for an IUS which, in effect, would be a request for Mirena. A breach of Clause 20.2 of the Code was ruled. The Panel did not consider that the circumstances warranted a ruling of a breach of Clauses 2 or 9.1.

The Panel considered that as the case studies on the Schering Health Care website only related to women using the IUS that section was not balanced. The company should have ensured that each type of LARC was represented by case studies. The material would encourage women to ask for the IUS which in effect would be a request for Mirena. The Panel ruled a breach of Clause 20.2. The Panel did not consider that the circumstances warranted a ruling of a breach of Clauses 2 or 9.1.

Proceedings commenced **10 December 2006**

Case completed **5 February 2007**

PRIMARY CARE TRUST HEAD OF MEDICINES MANAGEMENT v WYETH

Enbrel website advertisement

The head of medicines management at a primary care trust alleged that an advertisement for Enbrel (etanercept), marketed by Wyeth, which appeared on www.yahoo.com, constituted direct to consumer advertising. There was a small get-out clause buried on one of the inside pages of the advertisement, which stated that the message was only for the attention of US residents and that other countries had different regulations related to the use of medicines. However, by the time anybody reached that section they would have already read the advertisement that advised anybody with severe arthritis, and not getting sufficient relief, to ask their prescriber about Enbrel. This was clearly a breach of the Code.

The Panel noted that the yahoo.com website, which featured the first part of the Enbrel advertisement, was a US website – it referred *inter alia* to NBC and Dallas cowboys. The website was directed to a US audience. There was a separate Yahoo website for the UK and Ireland. Within the on-line advertisement at issue, readers were given the option to search, using ZIP code or state, for rheumatologists. Various pages of the advertisement stated 'This site is intended for US audiences only'. The advertisement had been placed by the US company not Wyeth UK.

The Panel considered that although accessible to anyone, the website at issue was directed to a US audience; further, the advertisement itself did not address a UK audience. The material was thus not directed to a UK audience and so the Panel ruled no breach of the Code. It was not an advertisement to the UK public for a prescription only medicine. No breach was ruled.

The head of medicines management at a primary care trust complained about an advertisement for Enbrel (etanercept), marketed by Wyeth Pharmaceuticals which appeared on www.yahoo.com on 13 December 2006.

COMPLAINT

The complainant alleged that this advertisement constituted direct to consumer advertising of Enbrel. There was a small get-out clause buried on one of the inside pages of the advertisement, which stated that the message was only for the attention of US residents and that other countries had different regulations related to the use of medicines. However, by the time anybody reached that section they would have already read the advertisement that advised anybody with severe arthritis, and not getting sufficient relief, to ask their prescriber about Enbrel. This was clearly a breach of the Code.

When writing to Wyeth the Authority asked it to respond in relation to Clauses 2, 9.1, 20.1 and 21 of the Code.

RESPONSE

Wyeth stated that the Enbrel advertisement on the yahoo.com website was authorised and placed there by its US affiliate, from 21 November 2006 to 21 December 2006, without the involvement or, indeed, knowledge of Wyeth UK. The advertisement was intended for a US audience only. Consequently, the advertisement did not specifically refer to the UK availability or use of the medicine.

A copy of the yahoo.com home page containing the website link to the Enbrel advertisement and a copy of the advertisement were provided together with a selection of pages linked to the advertisement. The various pages behind the link on the yahoo.com home page were US-specific. For example:

- to find a rheumatologist using the search service provided, either a US zip code or a US state needed be given. There was no option to select a different country. Further, the terms and conditions of use of this service referred to checking the physician's credentials with the American Medical Association, and stated, at the end, 'This site is intended for US audiences only';

- a US toll-free contact telephone number was given, to receive an Enbrel Information Kit;

- as was custom and practice with websites, links to the Terms of Use, Privacy Policy and other important information to which the website user was deemed to be bound, by virtue of using the website, was set out at the bottom of each Wyeth US web page. These made it clear that the Enbrel pages were only intended for a US audience. For example, in the Terms of Use there was a specific statement to this effect; the prescribing information was stated to be the US prescribing information and, before the full US prescribing information could be accessed, there was a statement that this information was intended for use only by US residents.

Wyeth submitted therefore, that as the advertisement did not refer to the availability or use of Enbrel outside of the US and did not specifically refer to its availability or use in the UK, the company had not

breached Clause 21.2 of the Code. Consequently, Wyeth did not accept that it had advertised Enbrel to the UK general public in breach of Clause 20.1.

Further, Wyeth submitted that in relation to the US advertisement at issue, it had maintained high standards at all times in compliance with Clause 9.1 and had done nothing to discredit or reduce confidence in the pharmaceutical industry in breach of Clause 2.

PANEL RULING

The Panel noted that the yahoo.com website, which featured the first part of the Enbrel advertisement, was a US website – it referred *inter alia* to NBC and Dallas cowboys. The website was directed to a US audience. There was a separate Yahoo website for the UK and Ireland. Within the on-line advertisement at issue, readers were given the option to search, using ZIP code or state, for rheumatologists. Various pages of the advertisement stated 'This site is intended for US audiences only'. The advertisement had been placed by the US company not Wyeth UK.

The Panel considered that although accessible to anyone, the website at issue was directed to a US audience; further, the advertisement itself did not address a UK audience. The material was thus not directed to a UK audience and so the Panel ruled no breach of Clause 21.1. It was not an advertisement to the UK public for a prescription only medicine. No breach of Clause 20.1 was ruled. Given these rulings it followed that there could be no breach of Clauses 2 and 9.1 and the Panel ruled accordingly.

Complaint received	**2 January 2007**
Case completed	**8 March 2007**

GLAXOSMITHKLINE v SANOFI PASTEUR MSD

Gardasil journal advertisement

GlaxoSmithKline complained about a journal advertisement for Gardasil (Human Papillomavirus Vaccine (types 6, 11, 16, 18) (Recombinant absorbed)) issued by Sanofi Pasteur MSD. Gardasil was indicated for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high grade vulvar dysplastic lesions (VIN 2/3), and external genital warts causally related to HPV types 6, 11, 16 and 18.

GlaxoSmithKline alleged that the claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was misleading, exaggerated and all embracing, implying that Gardasil had demonstrated efficacy to prevent cervical cancer (with all high-risk HPV types), when in fact it offered protection against two high-risk HPV types, 16 and 18 (around 70% of cervical cancers). This was not made clear and thus the advertisement was misleading and exaggerated the potential benefits of Gardasil in cervical cancer prevention.

The Panel noted that the summary of product characteristics (SPC) included data on the immune response to Gardasil which showed that overall, across all age groups, 99.9%, 99.8%, 99.8% and 99.6% of individuals who received Gardasil became anti-HPV6, anti-HPV11, anti-HPV16 and anti-HPV18 seropositive, respectively, one month after the third dose. The Panel noted that HPV types 16 and 18 were responsible for around 70% of cases of cervical cancer. The Panel considered that given the product's licensed indication the claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was not misleading or exaggerated as alleged. No breach of the Code was ruled.

The claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was immediately followed by the claim 'Benefit from 4 types – before and beyond cervical cancer'. GlaxoSmithKline alleged that the proximity and positioning of these two claims implied that Gardasil offered protection against four HPV types that played a causal role in cervical cancer when in fact it offered protection against two (HPV 16 and18). GlaxoSmithKline further alleged that the claim 'Benefit from 4 types – before and beyond cervical cancer' was ambiguous and its positioning immediately following 'Now there's Gardasil a vaccine that can prevent cervical cancer' was misleading.

The Panel noted that the claim 'Benefit from 4 types - before and beyond cervical cancer' appeared in a relatively small typeface beneath the bold, prominent claim, 'Now there's Gardasil a vaccine that can prevent cervical cancer' on the first page of the double page spread. The second page was headed 'The first vaccine that can prevent cervical cancer' beneath which 2 bullet points discussed the licensed indication of Gardasil and the HPV types 6, 11, 16 and 18. On balance, the Panel considered that in the context in which it appeared it was not entirely clear what the claim 'Benefit from 4 types - before and beyond cervical cancer' meant and in this regard it was ambiguous and misleading. A breach of the Code was ruled. However, the claim 'Benefit from 4 types - before and beyond cervical cancer' was subsequently subject to an appeal to the Code of Practice Appeal Board in a separate case, Case AUTH/1927/12/06, wherein the Appeal Board ruled no breach of the Code. The ruling in Case AUTH/1927/12/06 would apply and supersede the Panel's ruling in the present case, Case AUTH/1938/1/07. There had thus been no breach.

GlaxoSmithKline alleged that the claim 'Beyond the cervix, Gardasil can also prevent vulval pre-cancers and genital warts and reduce the incidence of vaginal pre-cancers caused by human papillomavirus types 6, 11, 16 or 18' incorrectly implied that each of the four HPV types played a causal role in each of the disease states listed.

The Panel did not consider that the claim implied that HPV types 6, 11, 16 and 18 all had a causal role in each of the conditions listed. In the Panel's view, most readers would assume that the conditions listed were caused by one or more of the HPV types listed. No breach of the Code was ruled.

GlaxoSmithKline UK Ltd complained about the promotion of Gardasil (Human Papillomavirus Vaccine (types 6, 11, 16, 18) (Recombinant absorbed)) by Sanofi Pasteur MSD Ltd. At issue was a double page advertisement (ref 10/06 09214c) which appeared in 'Doctor'.

GlaxoSmithKline explained that Gardasil was a quadrivalent vaccine against human papillomavirus (HPV) types 6, 11, 16 and 18. It was indicated for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high grade vulvar dysplastic lesions (VIN 2/3), and external genital warts causally related to HPV types 6, 11, 16 and 18.

There were approximately 15 'high-risk' (cancer-causing) HPV types. HPV 16 and 18 were responsible for around of 70% cervical cancers and the other high-risk types accounted for the remaining 30% of cases. HPV 16 and 18 also played a causal role in approximately 70% of high grade cervical dysplasias (CIN 2/3), 70% of high grade vulvar dysplasias (VIN 2/3) and the majority of high grade vaginal dysplasia (VaIN 2/3).

In contrast, HPV types 6 and 11 were 'low-risk' HPV types responsible for approximately 90% of genital warts; they were not responsible for cervical, vulvar or vaginal cancers or their respective high-grade dysplasias (also referred to as high-grade pre-cancers).

1 Claim 'Now there's Gardasil a vaccine that can prevent cervical cancer'

This claim appeared on the left-hand side of the double page spread.

COMPLAINT

GlaxoSmithKline alleged that this claim was misleading, exaggerated and all embracing, implying that Gardasil had demonstrated efficacy to prevent cervical cancer (with all high-risk HPV types), when in fact it offered protection against two high-risk HPV types, 16 and 18. As highlighted, HPV 16 and 18 accounted for around 70% of cervical cancers. Therefore, based on the available clinical data, Gardasil only had the potential to prevent 70% of cervical cancers. This was not made clear anywhere in the advertisement which was thus misleading and exaggerated the potential benefits of Gardasil in cervical cancer prevention. GlaxoSmithKline alleged breaches of Clauses 7.2 and 7.10.

RESPONSE

Sanofi Pasteur MSD pointed out that although it did not guarantee compliance with the Code, the advertisement was pre-vetted by the Medicines and Healthcare products Regulatory Agency (MHRA).

Sanofi Pasteur MSD noted that GlaxoSmithKline had correctly noted that Gardasil was indicated, amongst other things, to prevent cervical carcinoma (ie cervical cancer) causally related to HPV types targeted by the vaccine. Since HPV types 16 and 18 were responsible for around 70% of cases of cervical cancer it was a statement of fact and a true reflection of the indication that Gardasil could prevent cervical cancer. 'Can' in the claim, 'Now there's Gardasil a vaccine that can prevent cervical cancer', was chosen very carefully to ensure that that the claim reflected Gardasil's ability to prevent cervical cancer rather than the certainty that it would prevent cervical cancer.

Sanofi Pasteur MSD submitted that the claim simply stated the facts, Gardasil was available and indicated for the prevention of cervical cancer and therefore was not in breach of Clause 7.2 of the Code. Furthermore, through use of the word 'can', Sanofi Pasteur MSD had made specific efforts to ensure that the claim was not exaggerated. As a result there was no breach of Clause 7.10.

PANEL RULING

The Panel noted that Gardasil was licensed for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high grade vulvar dysplastic lesions (VIN 2/3), and external genital warts (condyloma acuminata) causally related to HPV types 6, 11, 16 and 18. Section 5.1 of the summary of product characteristics (SPC), Pharmacodynamic properties, discussed data on the immune response to Gardasil which showed that overall, across all age groups, 99.9%, 99.8%, 99.8% and 99.6% of individuals who received Gardasil became anti-HPV6, anti-HPV11, anti-HPV16 and anti-HPV18 seropositive, respectively, one month after dose three. The Panel noted that HPV types 16 and 18 were responsible for around 70% of cases of cervical cancer. The Panel considered that given the product's licensed indication the claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was not misleading or exaggerated as alleged. No breach of Clauses 7.2 and 7.10 was ruled.

2 Claim 'Benefit from 4 types – before and beyond cervical cancer'

This claim appeared on the left-hand page of the double page spread immediately below the claim in question at point 1 above.

COMPLAINT

GlaxoSmithKline noted that claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was immediately followed by the claim 'Benefit from 4 types – before and beyond cervical cancer'. The proximity and positioning of these two claims implied that Gardasil offered protection against four HPV types that played a causal role in cervical cancer when in fact it offered protection against two (HPV 16 and18). GlaxoSmithKline strongly disagreed with Sanofi Pasteur MSD's suggestion that the phrase 'before and beyond cervical cancer', made it very clear that it was referring to cervical intra-epithelial neoplasia, and vulval intra-epithelial neoplasia and genital warts, respectively. Sanofi Pasteur MSD also stated that the body of the advertisement contained expanded details relating to this statement. However, clarification in the body of the advertisement was not sufficient – the title claims should stand alone with regard to clarity. GlaxoSmithKline alleged that the claim 'Benefit from 4 types – before and beyond cervical cancer' was ambiguous and its positioning immediately following 'Now there's Gardasil a vaccine that can prevent cervical cancer' was misleading in breach of Clause 7.2.

RESPONSE

Sanofi Pasteur MSD noted that GlaxoSmithKline was concerned that this claim, and its position in the advertisement, was ambiguous and implied that Gardasil offered protection against four HPV types that were responsible for cervical cancer.

Sanofi Pasteur MSD submitted that this claim was not misleading. Section 4.1 of the SPC stated that Gardasil was indicated not just for the prevention of cervical cancer but also for the prevention of cervical dysplasia (pre-cancerous lesions that developed **before** cervical cancer itself), as well as diseases that occurred **beyond** the cervix (ie vulval intra-epithelial neoplasia, genital warts), all causally related to the four HPV types targeted by the vaccine. The statement reflected the benefits of Gardasil over and above protection against cervical cancer. The claim stood alone with regards to clarity and further details were provided in the right-hand side of the advertisement.

Similarly, Sanofi Pasteur MSD submitted that the claim was not ambiguous. As described above, the claim was not about cervical cancer but rather the other benefits of Gardasil that derived from the inclusion of four HPV types in the vaccine. Indeed, these two facts were linked by the inclusion of the hyphen.

For these reasons, Sanofi Pasteur MSD submitted that this claim was neither misleading, nor ambiguous, and was not in breach of Clause 7.2.

PANEL RULING

The claim 'Benefit from 4 types - before and beyond cervical cancer' appeared in a relatively small typeface beneath the bold, prominent claim considered above, 'Now there's Gardasil a vaccine that can prevent cervical cancer' on the first page of the double page spread. The facing second page of the advertisement was headed 'The first vaccine that can prevent cervical cancer' beneath which 2 bullet points discussed the licensed indication of Gardasil and the HPV types 6, 11, 16 and 18. The Panel considered that the claim 'Benefit from 4 types - before and beyond cervical cancer' was ambiguous. Some might consider that the four types referred to HPV types 6, 11, 16 and 18. Given the prominence of the preceding claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' and its reference to cervical cancer some readers might assume that the claim at issue implied that HPV types 6, 11, 16 and 18 each had a role in cervical cancer. It was only by reading the less prominent text in the bullet points on the facing page that the causative effects of the four HPV types became clear. Others might consider that term 'four' referred to the 4 licensed indications. On balance, the Panel considered that in the context in which it appeared it was not entirely clear what the claim 'Benefit from 4 types - before and beyond cervical cancer' meant and in this regard it was ambiguous and misleading. A breach of Clause 7.2 was ruled.

However, an earlier case, Case AUTH/1927/12/06 included a similar complaint about the claim 'Benefit from 4 types - before and beyond cervical cancer'. After the Panel had made its ruling in the present case an appeal in Case AUTH/1927/12/06 was considered by the Code of Practice Appeal Board which ruled no breach of Clause 7.2 of the Code as follows:

> **Appeal Board Ruling in Case AUTH/1927/12/06**
>
> The Appeal Board had some concerns that in the claim 'Benefit from 4 types – before and beyond cervical cancer', 'before … cervical cancer' related to time ie high-grade cervical dysplasia whereas 'beyond cervical cancer' related to anatomy ie vulva lesions or external genital warts. However the Appeal Board considered it unlikely that readers would assume that 'beyond' referred to a time after which a woman had developed cervical cancer given that the very prominent claim which preceded the claim at issue clearly referred to the prevention of cervical cancer.
>
> The Appeal Board did not consider that the claim implied that HPV types 6, 11, 16 and 18 all caused cervical cancer as alleged.
>
> Although noting its concern above, the Appeal Board considered that, in the context in which it appeared, the claim was not ambiguous or misleading and could be substantiated. No breach of Clauses 7.2 and 7.4 was ruled. The appeal was thus successful.

Although Case AUTH/1938/1/07 did not go to appeal (when the Panel made its ruling the appeal was pending), the Appeal Board's ruling of no breach of the Code would apply to the present case, Case AUTH/1938/1/07 superseding the Panel's ruling. There had thus been no breach.

3 Claim 'Beyond the cervix, Gardasil can also prevent vulval pre-cancers and genital warts and reduce the incidence of vaginal pre-cancers caused by human papillomavirus types 6, 11, 16 or 18'

This claim appeared on the right hand page of the double page spread.

COMPLAINT

GlaxoSmithKline alleged that this claim incorrectly implied that each of the four HPV types played a causal role in each of the disease states listed. Section 5.1 of the Gardasil SPC clearly defined the causal role of the high-risk (16 and 18) and low-risk (6 and 11) HPV types in the various disease states: 'HPV 16 and 18 are responsible for approximately… 70% of high-grade vulvar dysplasia (VIN 2/3)' and 'HPV 6 and 11 are responsible for approximately 90% of genital warts cases'. GlaxoSmithKline alleged that the claim was in breach of Clause 7.2.

RESPONSE

Sanofi Pasteur MSD submitted that the claim accurately reflected Section 5.1 of the SPC (sub-section titled 'Efficacy in subjects naïve to the relevant vaccine HPV type(s))' where only results for CIN 2/3 or adenocarcinoma in situ (AIS) were related to types 16 or 18 alone, whereas all other results were related to types 6, 11, 16 or 18.

The claim was therefore an accurate, balanced, fair, objective and unambiguous reflection of the data presented in the SPC and not in breach of Clause 7.2.

PANEL RULING

The Panel did not consider that the claim implied that HPV types 6, 11, 16 and 18 all had a causal role in each of the conditions listed. In that regard the Panel did not consider that the claim was misleading as alleged. In the Panel's view, most readers would assume that the conditions listed were caused by one or more of the HPV types listed. No breach of Clause 7.2 was ruled.

Complaint received	**2 January 2007**
Case completed	**6 March 2007**

COMMUNITY RESPIRATORY NURSE SPECIALIST v GLAXOSMITHKLINE

Promotion of Seretide Accuhaler

A community respiratory nurse specialist complained on behalf of an NHS trust about the conduct of a representative from GlaxoSmithKline and her promotion of Seretide Accuhaler 500mcg (salmeterol/fluticasone). The nurse also complained about a GlaxoSmithKline chronic obstructive pulmonary disease (COPD) audit programme.

Seretide was indicated, *inter alia*, for the symptomatic treatment of patients with severe COPD (FEV1 <50% predicted normal) and a history of repeated exacerbations, who had significant symptoms despite regular bronchodilator therapy.

The complainant noted that in October 2006 a GlaxoSmithKline representative told her that Seretide Accuhaler 500mcg was 'licensed' by the Scottish Medicines Consortium (SMC) to be used following treatment with short-acting bronchodilators in the management of COPD and that Symbicort Turbohaler [AstraZeneca's product] was not. The complainant accepted that the SMC advice for both medicines was worded differently but it was not a licence and did not specifically state that Seretide Accuhaler 500mcg could be used after short-acting bronchodilators.

The complainant stated that the information provided by the representative contrasted with the National Institute for Health and Clinical Excellence (NICE) Guideline on COPD (2004) which recommended the addition of an inhaled steroid in patients who were symptomatic despite treatment with short- and long-acting bronchodilators and/or who had FEV1 <50% and had had 2 exacerbations in 12 months requiring antibiotic or oral corticosteroids. At this point the representative failed to mention that this was in keeping with the information given in the GlaxoSmithKline summary of product characteristics (SPC) for Seretide, insisting instead that it was 'licensed' by the SMC to be used as previously stated.

The complainant noted that as the representative was so insistent she had double checked the SMC advice and website and found no evidence for the claim. When the complainant called the representative to ask for evidence for her SMC licence claims she became flustered and apologised if she had misled in anyway and that in fact she meant to say that 'whoever' granted the licence in the first instance stated that it could be used following treatment with short-acting bronchodilators. The complainant asked the representative to provide that evidence. A week later she provided a copy of the SPC.

The complainant stated that reports from several GPs and practice nurses led her to believe that the same information was being commonly given by GlaxoSmithKline representatives.

The Panel noted that the parties' accounts differed; it was difficult in such cases to know exactly what had transpired. 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 actually submit a complaint.

The Panel noted that the complainant referred to a discussion about SMC recommendations whereas the representative referred to a discussion about the UK licence. Given the complainant's position the Panel queried whether the representative had been sufficiently clear about the differences between Seretide and Symbicort and the differences between the SPC licensed indications and the SMC guidance.

The Panel noted that training material on the SPC for Seretide in COPD stated that Seretide 500 was aimed at patients who had had their second exacerbation. The training material stressed the two components to the licence ie FEV1 <50% predicted and that the patients still had symptoms even though they had had regular bronchodialator treatment, either long- or short-acting bronchodilators. The training material also stated that the Symbicort licence was more restrictive than Seretide's COPD licence as patients had to be tried on a long-acting bronchodilator before being put on Symbicort. The Panel queried whether when discussing the differences between the indications for Seretide and Symbicort the representatives were sufficiently clear about the similarities ie FEV1 <50% predicted and a history of repeated exacerbations.

Medicines had to be promoted in accordance with their SPCs. SMC and NICE guidance was occasionally different to the SPC indications.

Clearly it was of concern that the complainant had been taken aback by what she referred to as the representative's aggressive sales pitch and that colleagues had allegedly not been given all the details of the indications for Seretide in COPD. However it was not possible to determine where the truth lay. On the basis of the parties' submissions the Panel did not consider that there was sufficient evidence to show that on the balance of probabilities the representative had promoted Seretide outside its SPC or had failed to maintain a high standard of ethical conduct. The Panel ruled no breach of the Code.

The complainant also drew attention to an audit being conducted by GlaxoSmithKline; the audit report did not reflect the advice given in the NICE Guideline, (2004). The complainant was concerned that patients identified as priority patients (by a practice nurse or GlaxoSmithKline nurse advisor) might be unnecessarily prescribed or switched to Seretide.

The Panel noted that in Cases AUTH/1806/3/06 and AUTH/1809/3/06 it had considered a number of nurse audit schemes offered by GlaxoSmithKline including one in COPD. Overall the Panel considered that the services were not unacceptable and were not linked to the prescription of any specific medicine. The decision of what to prescribe lay with the patient's doctor. The services were not an inducement to prescribe, supply, administer, recommend or buy any medicine. No breach of the Code had been ruled.

Turning to the case now at issue, Case AUTH/1939/1/07, the Panel noted that the complaint related to the failure of material to reflect the NICE Guideline and that priority patients might be unnecessarily prescribed or switched to Seretide.

The Panel noted that the Code did not require arrangements for services to necessarily follow NICE guidelines. In general the Panel considered that services etc should not advocate use of medicines in a way that would be inconsistent with their SPCs.

The Panel noted GlaxoSmithKline's submission that the search criteria were agreed with the practice. The criteria were MRC dyspnoea score, FEV1, exacerbations within the last 12 months, smoking status, treatment inhaler technique, admissions, oxygen therapy and vaccination. The purpose of the audit was to identify patients that the practice might want to review. This could be done by the practice itself or using a GlaxoSmithKline service. The GlaxoSmithKline service if used would take place in line with an agreed practice protocol. The search identified patients already on combination treatments without identifying the product.

The audit report provided listed 20 priority patients, 16 of whom were currently taking a combination therapy; the report did not identify the patients other than by an identification number nor were details given about which combination therapy they were on. Of the fifteen patients with a recorded FEV1 result, 14 had an FEV1 <50% of predicted. The number of exacerbations in the last 12 months was noted for each patient and in this regard the audit report took account of the NICE Guideline which, unlike the Seretide SPC, put a time limit on exacerbations. None of the 20 patients had had an exacerbation of their disease in the last 12 months. The Panel queried whether it would be appropriate to prescribe Seretide given the lack of exacerbations within the last 12 months when Seretide's indication, *inter alia*, required patients to have repeated exacerbations.

The Panel considered that on the material before it there was insufficient evidence to show that on the balance of probabilities the audit service was an inducement to prescribe, supply, administer, recommend or buy Seretide. No breach of the Code was ruled.

A community respiratory nurse specialist complained on behalf of an NHS trust about the conduct of a representative from GlaxoSmithKline UK Ltd and her promotion of Seretide Accuhaler 500mcg (salmeterol/fluticasone). The nurse also complained about a chronic obstructive pulmonary disease (COPD) audit programme offered by GlaxoSmithKline.

Seretide was indicated, *inter alia*, for the symptomatic treatment of patients with severe COPD (FEV1 <50% predicted normal) and a history of repeated exacerbations, who had significant symptoms despite regular bronchodilator therapy.

COMPLAINT

The complainant noted that in October 2006 she was visited by a GlaxoSmithKline representative who stated that Seretide Accuhaler 500mcg was 'licensed' by the Scottish Medicines Consortium (SMC) to be used following treatment with short-acting bronchodilators in the management of COPD and that Symbicort Turbohaler [AstraZeneca's product] was not. The complainant accepted that the SMC advice for both medicines was worded differently but it was not a licence and did not specifically state that Seretide Accuhaler 500mcg could be used after short-acting bronchodilators. A breach of Clauses 3.2 and 7.4 was alleged.

The complainant stated that the information provided by the representative contrasted with the National Institute for Health and Clinical Excellence (NICE) Guideline on COPD (2004) which recommended the addition of an inhaled steroid in patients who were symptomatic despite treatment with short- and long-acting bronchodilators and/or who had FEV1 <50% and had had 2 exacerbations in 12 months requiring antibiotic or oral corticosteroids. At this point she failed to mention that this was in keeping with the information given in the GlaxoSmithKline summary of product characteristics (SPC) for Seretide, insisting instead that it was 'licensed' by the SMC to be used as previously stated. A breach of Clauses 3.2, 7.2 and 8.2 was alleged.

The complainant noted that as the representative was so insistent she had double checked the SMC advice and website the next day and found no evidence for the claim. The complainant called the representative and asked her to provide evidence for her SMC licence claims. She became rather flustered and apologised if she had misled in anyway and that in fact she meant to say that 'whoever' granted the licence in the first instance stated that it could be used following treatment with short-acting bronchodilators. The complainant asked the representative to provide that evidence. A week later she provided a copy of the SPC, dated 29 September 2006. The complainant alleged a breach of Clause 7.4.

The complainant stated that several GPs and practice nurses (who wished to remain anonymous) had reported that they had also been given this information by a GlaxoSmithKline representative (whom they would not identify) which sadly led the complainant to believe that this approach appeared to be commonly employed by local GlaxoSmithKline representatives. The complainant alleged a breach of Clause 2.

When writing to GlaxoSmithKline the Authority asked it to respond in relation to Clauses 9.1, 15.2 and 15.9 of the Code in addition to the clauses cited by the complainant.

RESPONSE

GlaxoSmithKline submitted that the representative had visited the complainant on a number of occasions, when the use of Seretide in both asthma and COPD had been discussed, and all these discussions had been amicable and professional. GlaxoSmithKline had also set up sponsored meetings for the complainant to network with other local practice nurses. On the occasion in question the representative distinctly remembered discussing differences in the UK licence between Seretide and Symbicort in COPD and, in particular, explaining that the Seretide licence allowed use after short-acting bronchodilators, whereas the Symbicort licence only allowed use after long-acting bronchodilators, as well as discussing the clinical evidence to support the Seretide licence. The representative did not recall any mention of the SMC as her objective for the call and the content of the discussion was entirely around the differences between the UK licences for Seretide and Symbicort.

GlaxoSmithKline submitted that during the week following the call, the representative received an email from the complainant (copy provided) which referred to a discussion about the 'SMC recommendation' (as opposed to licence) and the fact that the complainant had checked the SMC website, and actually stated that she 'couldn't find anything'. She went on to ask the representative to either forward a website address or a copy of the SMC document. The complainant did not refer to the NICE guideline in COPD. On receipt of the email the representative telephoned the complainant to explain that she had not referred to the SMC recommendations for Seretide but actually to the UK licence, apologised if she had confused the nurse, and offered to forward further information on the SPCs for both products to clear up the confusion. At this point the representative considered that the nurse was satisfied with her explanation and proposed course of action, and sent a return email (copy provided) to confirm these actions.

GlaxoSmithKline submitted that as promised the representative contacted medical information at GlaxoSmithKline and asked for further information on the respective licences for Seretide and Symbicort in COPD to be sent for her to pass on to the nurse. The representative called the nurse to arrange to drop off the relevant information, the respective SPCs and a Seretide in COPD Clinical Summaries pack, which she did when she visited the nurse at the end of October. At this point the nurse seemed satisfied and had no further questions.

UK licences for Seretide and Symbicort

The SPC for Seretide in COPD stated that 'Seretide is indicated for the symptomatic treatment of patients with severe COPD (FEV1 <50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular bronchodilator therapy', whereas the SPC for Symbicort in COPD stated that Symbicort was indicated for the 'symptomatic treatment of patients with severe COPD (FEV1 <50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators'.

GlaxoSmithKline submitted therefore that Seretide could be used in COPD after treatment with regular bronchodilators, ie either short- or long-acting bronchodilators. It was therefore appropriate to discuss the use of Seretide after regular use of short-acting bronchodilators. This was consistent with the representative call. In contrast, the licence for Symbicort in COPD stated explicitly that the product should be used after regular treatment with long-acting bronchodilators. This was an important difference between the products and it was appropriate for representatives to discuss this and make prescribers aware of the different patient populations appropriate for use of these products. Highlighting the fact that Seretide could be used in COPD after only short-acting bronchodilators, compared to Symbicort which could only be used in COPD after long-acting bronchodilators, as was done by the representative, was consistent with the SPCs for both medicines and appropriate.

SMC recommendations for Seretide and Symbicort

GlaxoSmithKline submitted that the SMC recommendation for Seretide in COPD stated merely that 'fluticasone/salmeterol (Seretide) is accepted for use within NHS Scotland for the treatment of patients with severe chronic obstructive pulmonary disease', and the SMC recommendation for Symbicort in COPD stated that 'budesonide/eformoterol (Symbicort) inhaler is accepted for use within NHS Scotland for treating patients with severe chronic obstructive pulmonary disease (COPD) who have significant symptoms despite regular therapy with long-acting bronchodilators'. Once again these recommendations highlighted the important difference between the patient populations appropriate for these products, and reflected their respective licences.

GlaxoSmithKline submitted that it and its representatives knew that SMC recommendations did not constitute a licence, but were in fact a national formulary which determined the use of products in Scotland. As the SMC recommendations made no restrictions on the prescribing of these medicines in Scotland, it was the UK licensed population within which it was appropriate to use these products.

Consequently, although not specifically stated, the SMC recommendation for Seretide would follow the UK licensed population and therefore Seretide was appropriate for patients after treatment with regular bronchodilators. It was therefore accurate to state that the SMC recommendation for Seretide in Scotland was that it was appropriate for treatment after short-acting bronchodilators.

With regard to the complainant's statement that the GlaxoSmithKline representative insisted that Seretide was licensed by the SMC to be used as previously stated, ie that it could be used following treatment with a short-acting bronchodilator, although the GlaxoSmithKline representative did not recall any discussions regarding SMC recommendations for Seretide, the SMC recommendations stated that Seretide should be used in the licensed population, and therefore after short-acting bronchodilators. Therefore although any such statement about a 'licence' would be technically inaccurate with regard to the legal status of the SMC as opposed to the competent authority in terms of responsibility for the grant of a licence, the clinical interpretation of such a statement would not be out of keeping with either the SMC recommendation or the Seretide SPC.

NICE Guideline for COPD

GlaxoSmithKline submitted that the NICE Guideline for COPD (2004) recommended an evidence-based approach to the management of stable COPD. In patients with breathlessness and exercise limitation, NICE initially recommended the use of a short-acting bronchodilator (either a β_2-agonist or an anti-cholinergic) as needed. In patients requiring further treatment, NICE recommended moving to a combined therapy with a short-acting β_2-agonist and a short-acting anti-cholinergic and then, if still symptomatic the use of a long-acting bronchodilator (either a β_2-agonist or an anti-cholinergic). NICE also made specific recommendations for patients with moderate or severe COPD who were still symptomatic despite the above therapies, and advocated the combination of an inhaled corticosteroid and a long-acting bronchodilator. However, NICE also made specific recommendations for frequent exacerbators and stated that inhaled corticosteroids should be prescribed for patients with an FEV1 ≤50% predicted, who had 2 or more exacerbations requiring treatment with antibiotics or oral corticosteroids in a 12 month period, and in its algorithm (provided) stated that these inhaled steroids should be added to optimised bronchodilator therapy with one or more long-acting bronchodilators.

Some difficulties arose because the NICE Guideline was not entirely consistent with the SPC for Seretide. (Additionally NICE guidance was not applicable in Scotland where this complaint had arisen.) Strict adherence to the NICE Guideline required that all patients with moderate or severe COPD (FEV1 ≤50%) only received Seretide when they had had 2 or more exacerbations requiring treatment with antibiotics or oral corticosteroids in a 12 month period and after having received both short- and long-acting bronchodilators. This recommendation was inconsistent with the Seretide SPC which was indicated in patients with FEV1 ≤50% who had a *history of repeated exacerbations* and were symptomatic de*spite regular treatment with bronchodilators*. Therefore, as there was no specified timeframe in the Seretide licence for patients to have had exacerbations, the NICE recommendation that Seretide should be used in patients who had 2 or more exacerbations over a period longer than 12 months was more restrictive than the SPC licence wording. As there was no specified type of bronchodilator which patients should have already received in the licence wording, the NICE recommendations were again more restrictive in this regard as Seretide was indicated in patients who had already received either a short- or a long-acting bronchodilator.

GlaxoSmithKline submitted that unfortunately there seemed to be some confusion on the part of the complainant in this regard as she stated that the NICE recommendation was in keeping with the information given in the Seretide SPC. This was not so since the Seretide SPC and the NICE Guideline clearly indicated that the product should be used in different patient populations. Nevertheless, the SPC took precedence over the NICE Guideline as promotion of a medicine must be in accordance with the terms of its marketing authorization and must not be inconsistent with the particulars listed in its SPC. However, since the patient population recommended in the NICE Guideline was more restricted than that indicated in the Seretide SPC, it was appropriate that whilst responsibly discussing the licensed population for Seretide, representatives also made prescribers aware of the NICE Guideline. Consequently, all primary care representatives had a leavepiece detailing the NICE recommendations and the position of combination treatments in the treatment pathway for use in discussions with health professionals, and in addition the non-promotional respiratory care team had the NICE Guideline included in their detail aid.

GlaxoSmithKline maintained that the representative did not discuss any licensing by the SMC, but rather the actual UK licences. The representative did not recall any discussion regarding SMC, and the email from the complainant referred to SMC recommendations. Furthermore, all discussion entered into by the representative was entirely within the UK licences and SPCs for both Seretide and Symbicort in COPD. The SMC had approved both Seretide and Symbicort for use in Scotland but had not commented further on the indicated population which remained as per the UK licence, therefore discussions of the UK licence were entirely appropriate in this regard. The NICE Guideline was not identical to the licence for Seretide, however it did not take precedence over the SPC and promotion of the licensed indication for Seretide was therefore appropriate, although it was right that representatives made prescribers aware of the NICE recommendations for combination treatments in COPD and appropriate training for representatives and suitable materials had been provided accordingly. Unfortunately, the complainant seemed to be slightly unsure as to the exact nature of the SMC recommendation as regards Seretide, and also the

consistency between the NICE Guideline recommendations and the SPC for Seretide. Furthermore, the complainant's recollection of events seemed to be somewhat different to both that of the representative, and her email to the representative following the call.

Consequently GlaxoSmithKline maintained that all promotion of Seretide by this representative was entirely within the licensed population and the indications of the SPC, therefore there was no breach of Clause 3.2. Furthermore, all the information provided by the representative in this call was in keeping with the Seretide SPC and it followed that all the information, claims and comparisons were accurate and based on an up-to-date evaluation of all the evidence, therefore there was no breach of Clause 7.2. Also, since all the information provided in this call was in keeping with the Seretide SPC all this information was capable of substantiation, therefore there was no breach of Clause 7.4.

GlaxoSmithKline submitted that throughout her career the representative had undertaken ongoing product and therapy training as set by the company and recently completed the GlaxoSmithKline annual certification test (copy provided), achieving the pass mark of 90% in all 3 therapy areas within which she worked. Over her time at GlaxoSmithKline the representative had undertaken various roles in the company and had never been the subject of an ABPI complaint. Since GlaxoSmithKline maintained that there had been no breach of any clause in the conduct of this representative during the call, and all representative activity was in line with the SPC it submitted that high standards had been maintained at all times by both GlaxoSmithKline and the representative and therefore there was no breach of either Clause 9.1 or 15.2. Furthermore, GlaxoSmithKline provided detailed representative briefing material regarding the licensed indication for Seretide and all representative training included information on the NICE Guideline and the licensed indications for other products used in COPD, and as a result there was no breach of Clause 15.9.

GlaxoSmithKline submitted that it was difficult to comment on the allegation that its representatives in the area had employed a general approach to mislead or present inaccurate information, without details of particular incidents. However, all representatives in the area had been trained and briefed on the same material and would be expected to discuss the same issues in any call with a health professional, ie the respective UK licences for Seretide and Symbicort, the use of Seretide in the treatment pathway of the NICE COPD Guideline and relevant SMC recommendations for use of Seretide in Scotland. There was no attempt by GlaxoSmithKline to mislead any practitioner or make inaccurate representations of licences or guidelines. GlaxoSmithKline was confident that the information presented by the representative in question had been shown to be accurate and in line with both the UK licence and SMC recommendations. Consequently GlaxoSmithKline did not accept any breach of Clause 2 in this regard.

FURTHER COMMENTS FROM THE COMPLAINANT

GlaxoSmithKline's response was sent to the complainant for comment.

The complainant stated that she had been visited by the representative on a few occasions prior to October. However there was only one main meeting which was an introductory meeting where the complainant's role was discussed at length. The purpose of other visits (not meetings) was to drop patient information leaflets, studies and to sign a request for placebo devices (all of which the complainant requested). All meetings and visits were amicable and professional. The use of and licence for Seretide was not discussed until October.

GlaxoSmithKline set up a sponsored meeting (not meetings) to help the complainant network with local practice nurses for which the complainant was very appreciative. She previously enjoyed mutually beneficial relations with pharmaceutical companies and representatives.

The complainant maintained that although the representative distinctly remembered discussing the differences between the UK licences for Seretide and Symbicort in COPD in October, the UK licence was never discussed at this point. The complainant distinctly remembered that only the SMC advice ('licence' was the term the representative used) and the NICE Guideline were discussed (NICE was only discussed because the complainant brought it up). The complainant remembered it clearly as she was taken aback by how aggressively the representative applied her sales pitch. Also, she was always very careful to ensure that representatives supplied evidence to support their claims. The complainant was the only community respiratory nurse specialist in the area and was relied upon to relay accurate information so she could not afford to miss important information or get confused.

The complainant stated there was evidence that she emailed the representative asking her to provide the SMC evidence to support her claim. The complainant did not refer to the NICE Guideline because she had a copy.

It was after this email that the representative telephoned and stated that it was not the SMC but 'whoever' granted the UK licence, the complainant requested a copy. The complainant sensed her anxiety at the complainant following through on her visit and the complainant was then convinced that she had made a deliberate attempt to mislead. The complainant did not discuss this with her.

The SPC and summaries pack was dropped off by the representative who did not stay to review the contents. However, had the complainant known she was going to provide a copy of the SPC the complainant could have saved her the trouble as she already had a copy. As the representative did not stay or follow up with a telephone call she would not have known if the complainant was satisfied.

Even though the claims could not be substantiated the complainant decided that she would speak to the representative and voice her discontent. However, during three education sessions colleagues voiced their surprise at the indications for the use of inhaled corticosteroids (the complainant's presentation contained scans of the SMC, SPC and NICE recommendations for Seretide and Symbicort) and commented that they had been told by a GlaxoSmithKline representative that Seretide could be used after short-acting bronchodilators in the management of COPD. The complainant asked if the representatives had mentioned FEV1 or exacerbations or the NICE Guideline and all said definitely not and realised that this was not an isolated incident and as these individuals did not want to get involved the complainant felt it her duty to make the complaint official.

As for the SMC advice and UK licence for Seretide and Symbicort the complainant was not confused regarding the differences. The complainant agreed that it was entirely appropriate for representatives to discuss the differences between the advice and licence and to discuss Seretide after regular short-acting bronchodilators provided the information was consistent with Clause 3.2 of the Code and did not differ or omit important product characteristics. In this instance the representative had said 'Seretide is licensed by the SMC to use after short-acting bronchodilators'.

The representative completely omitted important particulars listed in the SPC (FEV1 and exacerbations). The statement was economical with the truth and was misleading. It suggested that Seretide could be used if regular short-acting bronchodilators were ineffective regardless of FEV1 and exacerbations. This could result in inappropriate prescription.

Using the word 'licence' instead of advice indicated that it was absolute. Although the SMC advice was important it was only advice.

Mention of the NICE Guideline on COPD should have triggered the representative's memory and at this point she could have mentioned the UK licence and reviewed the small differences between them. The UK licence was never mentioned but instead she insisted that the SMC had 'licensed' Seretide to be used as previously stated. She was so insistent that the complainant doubted herself and that was why the complainant asked for the evidence.

The complainant would have had no problem if the representative had said 'Seretide is licensed to be used after short-acting bronchodilators for patients who have an FEV1 <50% and who have had repeated exacerbations'.

The complainant disagreed with GlaxoSmithKline on the point that the clinical interpretation of the SMC was not out of keeping with the SPC for Seretide. The SMC advice did not mention FEV1 % predicted (just severe disease) or exacerbations.

The complainant did not indicate that the NICE guidance was identical to the SPC, the complainant stated 'in keeping'. The NICE recommendations were only slightly different from the SPC for Seretide. NICE indicated FEV1 <50% and 2 exacerbations in 12 months whereas as the SPC indicated FEV1 <50% and repeated exacerbations.

As for the different patient population the complainant was not sure what was meant. If it referred to the NICE Guideline not being applicable in Scotland then the complainant disagreed. COPD pathology remained the same regardless of country. NHS Quality Improvement Scotland (QIS) usually adopted NICE advice. The local respiratory implementation pack and other documents had been copied from the NICE Guideline. It was a large body of evidence which could not be ignored. Obviously, GlaxoSmithKline agreed with this otherwise NICE recommendations would not be included in its materials.

The complainant did not question the training of the representative or the GlaxoSmithKline training programme. Presumably the inclusion of this section was to provide a character reference. The complainant had been a nurse for 20 years (respiratory specialist for 7 years) and had an excellent professional and academic record. The complainant was not sure that this had any bearing on this complaint.

The complainant stated that she was a plain speaker. This representative flatly denied that she discussed the SMC advice ('licence') so it was her word against the complainant's. The complainant stated she had nothing personal to lose or gain from the complaint and it was made with patients' best interests at heart. The complainant was not under any pressure to meet sales targets in an increasingly competitive market.

The complainant suggested that representatives carried some form of documentation that could be countersigned by the health professional agreeing what was discussed. The complainant did not think it was appropriate that information pertaining to the meeting was entered into a computer without her agreeing the content. The complainant suggested that this was a process open to abuse.

More and more health professionals were refusing to see pharmaceutical representatives and the complainant would be joining them regardless of the outcome of this complaint. This representative's (and other GlaxoSmithKline representatives') conduct had seriously undermined her confidence in the pharmaceutical industry.

The complainant believed that the representative had deliberately misquoted and omitted important information in an attempt to convince her that Seretide could be used earlier than indicated in the SPC. The complainant maintained that she breached the clauses listed in her complaint.

PANEL RULING

The Panel noted that the parties' accounts differed; it was difficult in such cases to know exactly what had transpired. 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 actually submit a complaint.

The Panel noted that the complainant referred to a discussion about SMC recommendations whereas the representative referred to a discussion about the UK licence. Given the complainant's position the Panel queried whether the representative had been sufficiently clear about the differences between Seretide and Symbicort and the differences between the SPC licensed indications and the SMC guidance.

The Panel noted the training material on the SPC for Seretide in COPD stated that Seretide 500 was aimed at patients who had had their second exacerbation. The training material stressed that there were two components to the licence ie FEV1 <50% predicted and that the patients still had symptoms even though they had had regular bronchodialator treatment, either long- or short-acting bronchodilators. The training material also stated that the Symbicort licence was more restrictive than Seretide's COPD licence as patients had to be tried on a long-acting bronchodilator before being put on Symbicort. The Panel queried whether when discussing the differences between the indications for Seretide and Symbicort the representatives were sufficiently clear about the similarities ie FEV1 <50% predicted and a history of repeated exacerbations.

Medicines had to be promoted in accordance with their SPCs. SMC and NICE guidance was occasionally different to the SPC indications.

Clearly it was of concern that the complainant had been taken aback by what she referred to as the representative's aggressive sales pitch and that colleagues had allegedly not been given all the details of the indications for Seretide in COPD. However it was not possible to determine where the truth lay. On the basis of the parties' submissions the Panel did not consider that there was sufficient evidence to show that on the balance of probabilities the representative had promoted Seretide outside its SPC or had failed to maintain a high standard of ethical conduct. The Panel ruled no breach of Clauses 3.2, 7.2, 7.4, 8.2, 9.1 and 15.2. It thus followed that there was no breach of Clause 2.

2 COPD Audit

COMPLAINT

The complainant drew attention to an audit being conducted by GlaxoSmithKline (sample audit report was provided); the report did not reflect the advice given in the NICE Guideline, (2004). The complainant was concerned that patients identified as priority patients (by a practice nurse or GlaxoSmithKline nurse advisor) might be unnecessarily prescribed or switched to Seretide. The complainant alleged a breach of Clauses 18.1 and 18.4.

RESPONSE

GlaxoSmithKline noted that the audit referred to was the part of the review service that was offered by GlaxoSmithKline that had already been the subject of complaint [Cases AUTH/1806/3/06 and AUTH/1809/3/06] and been found not in breach. The audit report provided by the complainant was a summary report of COPD patients for a practice generated by a search of the practice database using software installed by GlaxoSmithKline (Campbell or POINTS) as agreed by the practice. The search generated a report of COPD patients and had two purposes:

- it could highlight areas where the practice might like to improve data recording. For example the audit report provided showed that out of 131 patients, 121 had no record of an MRC dyspnoea score. This might highlight to the practice an area where it could improve patient records so it could better understand the profile of its COPD patients;

- it generated a summary report of priority patients, being those with worse symptoms, exacerbations, hospitalisations etc on which the practice might wish to focus its efforts, eg in a patient review, in order to improve patient care and reduce costs.

GlaxoSmithKline submitted that the database search was carried out after discussion with a non-promotional GlaxoSmithKline representative, the respiratory care associate (RCA). The RCA introduced and explained the GlaxoSmithKline patient review services which included use of software on the practice database to identify priority patients, and use of external health professionals (either local specialists or an agency nurse) to review patients if required by the practice. The practice was free to choose some, all or none of the review services on offer. The database search was the initial part of the review service and identified patients based on a range of criteria which could be seen in the summary report of priority patients. These criteria were: MRC dyspnoea score, FEV1, exacerbations, smoking status, treatment, inhaler technique, admissions oxygen therapy and vaccination. These criteria were set within the installed software but were agreed with and could be adjusted by the practice if required. The audit report was sent to the practice which could act on the results of the report entirely at its own discretion, including no further action, reviewing the patients themselves or engaging further in the GlaxoSmithKline review services by undertaking a specialist notes review or an agency nurse review.

GlaxoSmithKline submitted that the complainant had stated that the audit did not reflect advice given in the NICE Guideline. However, it was difficult to comment without further detail on where the complainant considered the advice was inconsistent since the NICE

Guideline did not state which patients should be identified as a priority. Neither, given the nature of this service and the use to which it was put, would GlaxoSmithKline see an absolute need for the listing to be consistent with the NICE Guideline. The criteria set by GlaxoSmithKline within the search were based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) COPD Guidelines and each search criteria could be referenced to advice recommendations within this initiative. Specifically the GOLD Guideline recommended ongoing monitoring and assessment of patients with COPD and as a part of this advice monitoring of:

- exposure to risk factors (smoking or environmental)
- disease progression and development of complications (symptoms eg dyspnoea and objective measures of lung function eg spirometry)
- pharmacotherapy (including a discussion of current therapeutic regimen and inhaler technique)
- exacerbation history (including severity, frequency and likely causes, as well as hospitalisations).

GlaxoSmithKline noted that the complainant was also concerned that this audit would identify patients that might be unnecessarily prescribed or switched to Seretide. However, it was not the purpose of this audit to identify patients that were suitable for Seretide. This audit report simply identified patients that the practice might want to review, whether it did review the patients or not was entirely up to the practice itself, as no further action was taken by GlaxoSmithKline on the basis of this report other than to provide it to the practice. If the practice wanted to review the patients then it could do this itself, or it could utilise the resources of the GlaxoSmithKline patient review service using a specialist notes review or nurse review service. However, if the patients were reviewed this was done entirely to an agreed practice protocol which might or might not include use of combination treatments and Seretide in particular.

GlaxoSmithKline submitted that as could be seen from the audit report itself, the search simply generated priority patients as described above. In addition, the search also identified patients that were already on combination treatments and did not identify which treatment the patient was on, so of the 16 patients identified as already taking a combination treatment, any or all of them could already be taking Seretide.

Consequently GlaxoSmithKline did not accept any breach of Clause 18.1 and 18.4 in the provision of this audit report as there was no inducement to prescribe, supply, administer, recommend, buy or sell any medicine in this service to medicine which was aimed entirely at enhancing patient care.

PANEL RULING

The Panel noted that in Cases AUTH/1806/3/06 and AUTH/1809/3/06 it had considered a number of nurse audit schemes offered by GlaxoSmithKline including one in COPD. Overall the Panel considered that the services were not unacceptable and were not linked to the prescription of any specific medicine. The decision of what to prescribe lay with the patient's doctor. The services were not an inducement to prescribe, supply, administer, recommend or buy any medicine. No breach of Clauses 18.1, 9.1 and 2 of the 2003 Code had been ruled.

Turning to the case now at issue, Case AUTH/1939/1/07 the Panel noted that the complaint related to the failure of material to reflect the NICE Guideline and priority patients might be unnecessarily prescribed or switched to Seretide.

The Panel noted that the Code did not require arrangements for services to necessarily follow NICE guidelines. In general the Panel considered that services etc should not advocate use of medicines in a way that would be inconsistent with their SPCs.

The Panel noted GlaxoSmithKline's submission that the search criteria were agreed with the practice. The criteria were MRC dyspnoea score, FEV1, exacerbations within the last 12 months, smoking status, treatment inhaler technique, admissions, oxygen therapy and vaccination. The purpose of the audit was to identify patients that the practice might want to review. This could be done by the practice itself or using a GlaxoSmithKline service. The GlaxoSmithKline service if used would take place in line with an agreed practice protocol. The search identified patients already on combination treatments without identifying which product the patient was on.

The audit report provided listed 20 priority patients, 16 of whom were currently taking a combination therapy; the report did not identify the patients other than by an identification number nor were details given about which combination therapy patients were on. Of the fifteen patients with a recorded FEV1 result, 14 had an FEV1 <50% of predicted. The number of exacerbations in the last 12 months was noted for each patient and in this regard the audit report took account of the NICE Guideline which, unlike the Seretide SPC, put a time limit on exacerbations. None of the 20 patients had had an exacerbation of their disease in the last 12 months. The Panel queried whether it would be appropriate to prescribe Seretide given the lack of exacerbations within the last 12 months when Seretide's indication, *inter alia*, required patients to have repeated exacerbations.

The Panel considered that on the material before it there was insufficient evidence to show that on the balance of probabilities the audit service was an inducement to prescribe, supply, administer, recommend or buy Seretide. No breach of Clauses 18.1 and 18.4 was ruled.

Complaint received 2 January 2007

Case completed 23 April 2007

CASE AUTH/1940/1/07

GENERAL PRACTITIONER v BAYER

Avelox leavepiece

A general practitioner complained about the front cover of an Avelox (moxifloxacin) leavepiece, issued by Bayer, which stated 'In chest infections, when your first reaction is concern, your first choice should be Avelox'. The complainant was extremely concerned about the message given; obviously Avelox, as a newly developed antibiotic, should not be used in first line therapy. She alleged that the message was misleading.

The Panel noted that the claim advocated the use of Avelox in the treatment of chest infections which caused concern. In the Panel's view such chest infections would include severe cases of community acquired pneumonia for which Avelox was not licensed. The Panel further noted that the Avelox summary of product characteristics (SPC) did not categorically state that the antibiotic should not be used first line although it did state that consideration should be given to official guidance on the appropriate use of antibacterial agents. Thus whilst the claim 'Your first choice should be Avelox' was not inconsistent with the particulars listed in the SPC it implied that Avelox was the first choice ie it was the only first choice. The Panel considered that the claim was misleading and a breach of the Code was ruled.

A general practitioner complained about a leavepiece (ref 6AVEL53) for Avelox (moxifloxacin) issued by Bayer plc, Pharmaceutical Division.

COMPLAINT

The complainant noted that the front cover stated 'In chest infections, when your first reaction is concern, your first choice should be Avelox'. She was extremely concerned about the message that was being given; obviously Avelox, as a newly developed antibiotic, should not be used in first line therapy. She considered that the message given by the advertisement was quite misleading.

When writing to Bayer, the Authority asked it to respond in relation to Clause 7.2 of the Code.

RESPONSE

Bayer stated that the leavepiece was given to primary care health professionals by its representatives. Bayer considered the claim at issue was consistent with the marketing authorization. Avelox was a fluoroquinolone antibiotic, launched in the UK at the end of March 2003. It was licensed for the treatment of acute exacerbations of chronic bronchitis, community acquired pneumonia (except severe cases) and acute bacterial sinusitis (adequately diagnosed).

There was no specification within the marketing authorization as to where Avelox should be positioned in the treatment of chest infections.

Bayer considered that Avelox was promoted in a clinically appropriate manner; the company had taken great care to ensure that all advertising relating to Avelox was accurate, fair and reflected the evidence clearly.

Bayer did not believe that the claim 'In chest infections, when your first reaction is concern, your first choice should be Avelox' was in breach of Clause 7.2 of the Code.

PANEL RULING

The Panel noted that the claim advocated the use of Avelox in the treatment of chest infections which caused concern. In the Panel's view such chest infections would include severe cases of community acquired pneumonia for which Avelox was not licensed. The Panel further noted that the Avelox summary of product characteristics (SPC) did not categorically state that the antibiotic should not be used first line although it did state that consideration should be given to official guidance on the appropriate use of antibacterial agents. Thus whilst the claim 'Your first choice should be Avelox' was not inconsistent with the particulars listed in the SPC it implied that Avelox was the first choice ie it was the only first choice. The Panel considered that the claim was misleading. A breach of Clause 7.2 was ruled.

Complaint received	4 January 2007
Case completed	2 February 2007

CASE AUTH/1942/1/07

MEMBER OF THE PUBLIC v JANSSEN-CILAG

Disease awareness campaign on schizophrenia.

A member of the public complained about a schizophrenia advertisement placed by Janssen-Cilag in the Big Issue magazine. The advertisement told readers, *inter alia*, that 'Schizophrenia can be very difficult to live with. But the good news is, with modern treatments there's now a real chance of recovery. So it's very important to discuss with your doctor the choices available'.

Janssen-Cilag produced Risperdal (risperidone) and Risperdal Consta (long acting risperidone for intramuscular injection), an atypical antipsychotic.

The complainant alleged that the claim 'the good news is, with modern treatments there's now a real chance of recovery' was misleading and untrue. There was an implied association between visiting the doctor to discuss choices and the modern treatments available from Janssen-Cilag.

The advertisement led to a website (oneinonehundred.co.uk) sponsored by Janssen-Cilag which the complainant alleged promoted a prescription-only medicine as 'long acting injections' was underlined twice, and 'atypical antipsychotics' was underlined three times. This underlining re-reinforced the link between long-lasting injections and atypical antipsychotics. The complainant noted that Risperdal Consta was the only atypical antipsychotic available as a long-acting injection.

The complainant alleged that the statement on the website that atypical antipsychotics were superior to the old-fashioned ones, was not true. Readers were encouraged to 'ask your doctor if any of the newer treatments for schizophrenia would be suitable for you'. No antipsychotics were benign: their adverse effects were more severe than the condition for which they were prescribed. This applied as much to atypical as to the old-fashioned antipsychotics.

The complainant alleged that the claim 'schizophrenia is a disease of the mind', was not proven. The website also stated 'abnormalities in the transfer and processing of information within the brain' were related to schizophrenia; this was not true.

The complainant alleged that the claim that medicines would reduce the risk of further illness was also untrue, since Janssen-Cilag had stated the importance of not stopping the medicine once started on it.

The complainant noted the Brainchip link on the website, a cartoon of a man with a chip in the middle of his brain, was a link to a cartoon serial about schizophrenia. Given the very recent approval of vagus nerve stimulation (VNS) in the US for depression, and the European approval of VNS in epilepsy, depression and bi-polar disorder, this link within the site was deeply sinister; it was an attempt to condition patients with schizophrenia to the possibilities of 'pace-makers for the mind', ie neuroleptics delivered direct to the brain by surgical implant, in the not too distant future.

The Panel noted that the advertisement had been published in the lay press. Schizophrenia was a chronic condition. The Panel considered that some lay people, particularly those who knew very little about schizophrenia, might assume that recovery meant elimination of the illness, particularly as the advertisement referred to a 'real chance' of recovery in the context of 'modern treatments' and described this as 'good news'. The advertisement was misleading in this regard. A breach of the Code was ruled.

The Panel noted that whilst the advertisement referred to modern treatments there was no direct or implied reference to a specific medicine. There were several 'modern' treatment choices. The Panel did not consider that the statement at issue promoted a specific prescription only medicine to the public or would encourage patients to ask their health professional to prescribe a specific prescription only medicine. No breach of the Code was ruled.

The Panel noted that throughout the website certain terms such as 'psychiatrist', 'diagnosis' and 'mental health team' were underlined. These links led to a glossary where an explanation was given. In a section headed 'Newer medications' the phrase 'atypical antipsychotics' was underlined in a sentence which mentioned their mechanism of action and effect on a broader range of symptoms than older medications. The phrase 'long-acting injections' was underlined in the final sentence of the same section which listed the various presentations available. The reference to short-acting injections was not underlined. 'Long-acting injections' was also underlined in the preceding paragraph which dealt with older medications. The Panel noted that Janssen-Cilag's product, Risperdal Consta was the only atypical available as a long-acting injection. Given the format of the site wherein various terms were underlined throughout, the Panel did not consider that the underlining of the phrases at issue was inappropriate. It did not give them undue emphasis such that they either promoted a prescription only medicine to the general public or encouraged members of the public to ask for a specific medicine, as alleged. No breach of the Code was ruled.

The Panel noted that one of the 'Ten Tips to Help you Discuss Treatment with your Doctor' was 'Ask your doctor if any of the newer treatments for schizophrenia would be suitable for you especially if you have had distressing side effects with other

treatments'. The side effect section which appeared earlier in the website explained that the risk of certain side effects associated with newer medicines was much lower but not totally absent. The Panel did not consider the bullet point at issue inferred that atypical antipsychotics were benign and thus superior to older medication as alleged. The website made it clear that side effects were associated with the newer medicines. No breach of the Code was ruled.

The Panel did not consider that the description of schizophrenia as a 'disease of the mind' and references to abnormalities in the transfer and processing of information within the brain were unacceptable as alleged. The section 'Possible causes of Schizophrenia' explained that for the majority of people treatment relied on medicines which modified the effects of the neurotransmitters in the brain. It was also clearly stated that there was no known single cause of schizophrenia. The Panel did not consider that the phrase a 'disease of the mind' was unacceptable as alleged. No breach of the Code was ruled.

The section 'The effect of discontinuing treatment' included the claim 'Antipsychotic drugs reduce the risk of future illness in patients who have recovered from an acute episode'. The claim did not refer to 'further illness' as stated by the complainant. The Panel did not consider that the claim as published on the website was untrue as alleged. The effect of discontinuation of treatment and relapse rates were discussed. It was made clear that even with continued treatment patients might relapse. No breach of the Code was ruled.

The Panel noted that the Brainchip link on the website led to a self-help book for people experiencing psychosis. The booklet was produced with support from Janssen-Cilag. The booklet discussed treatment but did not mention a specific medicine or class of products. The Panel did not consider that it was an attempt to condition schizophrenic patients to the possibility of neuroleptics being delivered straight to the brain by surgical implant as alleged. The computer chip in the cartoon was depicted as a negative aspect of the patient's delusion rather than as part of the solution. No breaches of the Code were ruled.

In considering the campaign as a whole the Panel noted that the material was biased towards atypical antipsychotics ie the newer more modern treatments for schizophrenia. There were however, several atypical agents available. Nonetheless the Panel had some concerns about the bullet point 'Ask your doctor if any of the newer treatments for schizophrenia would be suitable for you especially if you have had distressing side effects with other treatments'. Whilst the atypical antipsychotics might be a rational treatment choice for newly diagnosed patients or those unable to tolerate the older agents, some patients would be satisfactorily controlled on their current treatment such that it would not be prudent to switch them to atypicals and risk a loss of control in the process. The bullet point seemed to open up that possibility to the patient although the final decision would always lie with the prescriber. Although noting its concerns the Panel, however, did not consider that either the advertisement or the website had failed to maintain a high standard; no breaches of the Code were ruled.

A member of the public complained to the Medicines and Healthcare products Regulatory Agency (MHRA) about an advertisement issued by Janssen-Cilag Ltd and sent a copy of her letter to the Authority. The advertisement (RISP/R/06-0108), published in the Christmas 2006 edition of the Big Issue, featured the statement 'Schizophrenia strikes one in one hundred ... and affects many more'. Beneath an image of a painting the advertisement continued '... but the picture's looking brighter. Schizophrenia can be very difficult to live with. But the good news is, with modern treatments there's now a real chance of recovery. So it's very important to discuss with your doctor the choices available'.

Janssen-Cilag produced Risperdal (risperidone) and Risperdal Consta (long acting risperidone for intramuscular injection), an atypical antipsychotic.

COMPLAINT

The complainant alleged that the claim 'the good news is, with modern treatments there's now a real chance of recovery' was misleading. It was simply not true that modern treatments ie atypical antipsychotics such as Risperdal and Risperdal Consta, led to recovery. Readers were exhorted to discuss with their doctor the choices available. There was an implied association between visiting the doctor to discuss choices and the modern treatments available, which would of course be prescribed treatments supplied by Janssen-Cilag.

The advertisement led to a website (oneinonehundred.co.uk) sponsored by Janssen-Cilag which the complainant alleged promoted a prescription-only medicine by underlining 'long acting injections' twice, and 'atypical antipsychotics' three times. Clicking on these underlined words revealed an explanation of the term. No other terms were so underlined. This underlining re-reinforced the link between long-lasting injections and atypical antipsychotics. The complainant noted that Risperdal Consta was the only atypical antipsychotic available as a long-acting injection.

The complainant alleged that other false statements on the website were that atypical antipsychotics were superior to the old-fashioned ones. This was not true. Readers were encouraged to 'ask your doctor if any of the newer treatments for schizophrenia would be suitable for you'. No antipscychotics were benign: their adverse effects were more severe than the condition for which they were prescribed. This applied as much to atypical as to the old-fashioned antipsychotics.

The complainant alleged that the claim 'schizophrenia is a disease of the mind', was not proven. The website also stated 'abnormalities in the transfer and processing of information within the brain' were related to schizophrenia; this was not true.

The complainant alleged that the claim that medicines

would reduce the risk of further illness was a lie, since Janssen-Cilag had also stated the importance of not stopping the medicine once started on it. The effect of rapid withdrawal from antipsychotics was becoming increasingly publicised. It was precisely these effects which were cleverly utilised in the original trials prior to the licensing of risperidone.

The complainant noted that the Brainchip link on website, a cartoon of a man with a chip in the middle of his brain, was a link to a cartoon serial about schizophrenia which could be downloaded. Given the very recent Food and Drug Administration (FDA) approval of vagus nerve stimulation (VNS) for depression, as of July 2005, and the European approval of VNS for use in epilepsy, depression and bi-polar disorder, this link was deeply sinister. This was a blatant attempt to condition patients with schizophrenia to the possibilities of 'pace-makers for the mind', ie neuroleptics delivered direct to the brain by surgical implant in the not too distant future.

When writing to Janssen-Cilag the Authority asked it to respond in relation to Clauses 2, 9.1, 20.1 and 20.2.

RESPONSE

Janssen-Cilag submitted that its 1 in 100 campaign was a public health awareness campaign which was consistent with the provisions of Clause 20.2. The supplementary information to Clause 20.2 stated that 'A company may conduct a disease awareness or public heath campaign provided that that the purpose is to encourage members of the public to seek treatment for their symptoms while in no way promoting the use of a specific medicine'. The wording within the advertisement 'So it's very important to discuss with your doctor the choices available' was consistent with these principles.

Although Janssen-Cilag supported the 1 in 100 campaign it was not developed in isolation. The campaign had received considerable support from numerous patient advocacy groups and was launched at the House of Commons with a keynote address given by an MP and attended by a health minister. In addition, the campaign materials were included as an example of best practice, by the ABPI Informed Patient Initiative Taskforce in the evidence submitted to the Informed Patient Work Stream of the European Union high level Pharmaceutical Forum in May/June 2006.

Janssen-Cilag noted that to date over 20,000 brochures (containing the information on the website) had been distributed; the website itself had received over 13,500 hits since July 2006 (more than 2000 per month) and of 234 feedback cards only 6 had negative comments. This showed how useful users and carers had found the campaign. Janssen-Cilag submitted that based on this type of feedback, as well as input it received during the development of the initiative, it was providing a balanced and factual health awareness campaign for the public.

Janssen-Cilag stated that the initiative was developed in conjunction with both service users and carer groups as well as service providers and various MPs. As such it had incorporated input from diverse and influential groups of people. It aimed to give patients, their families and friends information about schizophrenia and the range of treatments available. Discussion of treatments was not limited to pharmacological interventions, but also discussed psychosocial treatments. With regard to pharmacological interventions, typical and atypical antipsychotics were referred to in a fair and balanced way with advantages and disadvantages for each being clearly stated. The initiative promoted informed choice, and this aspect also featured prominently within the National Institute for Health and Clinical Excellence (NICE) guidance. This was in keeping with its educational objective, and the campaign encouraged patients to discuss the choices available with their doctor. The campaign did not encourage the use of, nor encourage patients to ask their doctor for a specific medicine.

Janssen-Cilag submitted that as well as helping patients to make informed choices (in conjunction with their doctor) the initiative also encouraged patients to discuss treatment options with their care workers and helped to decrease the stigma associated with schizophrenia.

Janssen-Cilag noted that the complainant had alleged that the claim 'the good news is, with modern treatments there's now a real chance of recovery' was misleading and that it was not true that modern treatments ie atypical antipsychotics such as risperidone led to recovery, Janssen-Cilag submitted that within the context of psychiatry, and specifically schizophrenia, recovery did not imply a cure. Schizophrenia was a life-long chronic mental illness, however with the use of modern treatments (the use of the word 'modern' did not exclusively mean atypical antipsychotics, rather current treatment options, pharmacological or otherwise) there might be restoration to a former or better condition. Certainly, various government initiatives regarding schizophrenia were aimed at recovery, with the focus being on recovery of social function for example, as opposed to elimination of the illness altogether. Indeed, the concept of recovery was accepted as being applicable to people with psychosis and was endorsed by the Department of Health (DoH) in a positive way (The Journey to Recovery – the government's vision for mental health care. DoH, November 2001). There were numerous definitions of recovery that did not equate with cure and were focussed for example, on patients returning to work, to independent living or towards having more meaningful relationships (Liberman *et al* 2002).

Three views of recovery from independent sources were:

1 'Recovery can be defined as a personal process of tackling the adverse impacts of experiencing mental health problems, despite their continuing or long-term presence. It involves personal development and change, including acceptance that there are problems to face; a sense of involvement and control over one's life; and the cultivation of hope and using support from others.' (Rethink website)

2 'The vast majority [of patients] have real prospects of recovery - if they were supported by appropriate services, driven by the right values and attitudes.' (DoH. The journey to recovery: the government's vision for mental health care)

3 'The 1 in 100 campaign fits closely to current government policies as reflected in the National Service Framework and NICE guidelines on schizophrenia. Both these sources show that there is now a very strong evidence base that care programmes and new drug therapies can secure recovery for many patients.' (Letter from a Professor at Imperial College London to Janssen-Cilag, January 2007)

Janssen-Cilag submitted therefore that the article was not misleading within the context of schizophrenia and was consistent with the aims and objectives of modern treatment regimens.

Janssen-Cilag noted the complainant's allegation there was an implied association between visiting the doctor to discuss choices and the modern treatments available. Janssen-Cilag submitted that the statement ' … discuss with your doctor the choices available' encouraged patients to go to their doctors and discuss the treatment choices which might include psychosocial as well as pharmacological treatment options. This statement was not inconsistent with the requirements of Clause 20.2 that allowed disease awareness campaigns to be undertaken provided that they encouraged members of the public to seek treatment for their symptoms, but did not promote the use of a specific medicine. Indeed, there was no mention of any medicine anywhere within the advertisement, which encouraged discussion between the patient and their doctor regarding treatment options.

Janssen-Cilag submitted that patient choice featured prominently on the government's agenda for management of mental health issues (National Service Framework for Mental Health: Modern Standards & Service Models. National Health Service / DoH September 1999) and certainly NICE guidance encouraged patient choice and full discussion of the treatment options available. NICE even recommended advanced directives so that the patient's wishes might be taken into account if they were unable to discuss options with their doctor eg because of an acute psychotic episode. Furthermore, Rethink issued a statement in December 2006 in support of patient choice (Pinfold 2006).

Janssen-Cilag submitted that there was no mention of a Janssen-Cilag product (or any other product) within the article and it denied that it had encouraged members of the public to ask their doctor for a specific medicine, or that it had promoted a prescription only medicine to the public.

Janssen-Cilag noted that the complainant had alleged that the website promoted a prescription only medicine underlining certain phrases.

Janssen-Cilag submitted that the website provided fair and balanced information about schizophrenia, its possible causes, symptoms, and both pharmacological and psychosocial treatments. The website stated in a succinct and understandable manner the positive aspects as well as potential side effects of the typical and atypical antipsychotics. All of the above would help the patient to have a more informed discussion with their doctor about the treatment choices available.

Janssen-Cilag explained that in response to a request from carers and users, underlined terms on the website provided links to a glossary where an explanation was given of the word in question. The terms were certainly not all treatment options eg mental health teams was underlined as was the word psychiatrist. To infer that this was a method of linking long-lasting injections and atypical antipsychotics was without grounds in view of the variety of other words also underlined.

Janssen-Cilag noted also that the complainant referred to the fact that Risperdal Consta was the only atypical antipsychotic available as a long-acting injection. Within the context of the broad range of information provided within the web-site there was no undue emphasis upon this particular treatment option. Indeed whether a patient was willing to accept a medicine by injection was part of any discussion about treatment options and acceptability that a doctor would have with their patients. There were also other medicines which could be given by a long-acting injection.

Janssen-Cilag therefore submitted that it had not promoted a prescription only medicine to the general public, and specifically that it had not promoted the use of Risperdal Consta to members of the general public.

Janssen-Cilag rejected the allegation that it had promoted atypical antipsychotics as superior to the old-fashioned ones. Both types of antipsychotics were important treatment options and selection depended on the individual patient and desired therapeutic outcome. Janssen-Cilag presented the potential advantages and disadvantages of each in a considered and balanced way. Other independent bodies such as NICE, however, specifically recommended that an atypical antipsychotic should be considered for a newly diagnosed patient.

Janssen-Cilag agreed with the complainant's view that no antipsychotic was benign. Indeed Janssen-Cilag had noted side effects that might occur with the different classes, but refuted the claim of bias towards atypical antipsychotics.

Janssen-Cilag submitted that the complainant was wrong to conclude that it had encouraged patients to request atypicals from their doctor. Janssen-Cilag had simply advocated patient choice where possible, and it did not comment in this respect on whether antipsychotics were benign or otherwise: indeed it was widely accepted that antipsychotics (whether these be typical or atypical) were associated with significant side effects.

Janssen-Cilag submitted that when referring to newer treatments it had included in this definition psychological therapies including cognitive behavioural therapy. The Layard Report recommended a wider use

of psychosocial treatments in mental health and there was an increasing evidence base for this.

In relation to the statement that schizophrenia was a 'disease of the mind' on the website, Janssen-Cilag submitted that it was widely accepted that schizophrenia was a neuro-developmental disorder of the brain leading to thought disorder. The dopamine hypothesis might account for the development of positive and negative symptoms of schizophrenia, although other hypotheses involving various other neurotransmitters also existed (Carlsson *et al* 1997).

Janssen-Cilag submitted that the statements on the website were therefore not inconsistent with these hypotheses. The word mind was widely accepted as meaning the human consciousness that originated in the brain and was manifested especially in thought, perception, emotion, will, memory and imagination. Many of these functions were affected in patients with schizophrenia and to de-link mind and brain would be incorrect. Importantly, the word mind would be more acceptable to patients and carers than the word brain.

In relation to the allegation that the claim that medicine would reduce the risk of further illness was a lie, Janssen-Cilag submitted that it was widely accepted in mental health that medicines reduced the risk of further illness, provided they were taken regularly. There was published evidence to support this for both typical and atypical antipsychotics, from placebo-controlled studies and discontinuation studies (Schooler 1993, Davis *et al* 1993). NICE considered that pharmacological intervention was important to prevent relapse. Whilst it stated that around 20% of patients might only have one episode, it recommended that, as there was no reliable predictor of prognosis or drug response, pharmacological prevention of relapse should be considered for every patient with schizophrenia. Published evidence established the efficacy of antipsychotics in the prevention of relapse.

Janssen-Cilag submitted in respect of the complainant's comment regarding clever utilisation of data in clinical trials prior to the licensing of risperidone, it observed that the marketing authorization for risperidone was granted following an independent and comprehensive review of the efficacy and safety data submitted to the relevant competent authority.

In relation to the allegations about the link between the Brainchip website link and recent FDA approval for VNS, Janssen-Cilag submitted that the Brainchip link on the website was taken directly from a book called 'The Secret of the Brain Chip' by a psychiatrist which was first published 6 years ago. It included a cartoon of a man with a microchip in the middle of this brain and the purpose was to depict an example of a possible delusion a patient might experience with schizophrenia. This book had been used extensively with many of the early intervention services and young carers, and although its style might not be suitable for all individuals, Janssen-Cilag aimed to provide a wide range of different styles of material to enable patients and health professionals to choose which they might use to obtain further information about schizophrenia. This cartoon had absolutely no association with the recent FDA approval for VNS; Janssen-Cilag was not able to comment further about the complainant's view of this.

In conclusion, Janssen-Cilag refuted any breach of Clauses 20.1 and 20.2; furthermore it also refuted the allegations made by the complainant in respect of the said article and related web-site. With respect to the development of the 1 in 100 campaign and associated materials Janssen-Cilag had undertaken due diligence around the content such that it had maintained high standards and not brought the industry into disrepute. Janssen-Cilag therefore denied a breach of either Clause 9.1 or Clause 2.

Janssen-Cilag submitted that in replying it had considered the views expressed by the complainant very carefully, and without prejudice to the views expressed above, would take these views into consideration in future communications with the general public.

PANEL RULING

The Panel noted that the advertisement had been published in a journal where it would be read by members of the public. Clause 20.1 prohibited the promotion of prescription only medicines to the general public. Clause 20.2 stated, *inter alia*, that information made available to the general public about prescription only medicines must be factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment. Statements must not be made for the purpose of encouraging members of the public to ask their health professional to prescribe a specific prescription only medicine.

The Panel noted that beneath a reproduction of a painting by a patient the advertisement read '… but the picture's looking brighter'. This was followed by less prominent text that read 'Schizophrenia can be very difficult to live with. But the good news is, with modern treatments there's now a real chance of recovery'.

The Panel noted Janssen-Cilag's submission that there were numerous definitions of recovery which did not equate to a cure. These included restoration to a better condition or independent living. The Panel noted the varying definitions but considered that given the intended audience it was important to be extremely clear about what was meant by 'recovery'. Schizophrenia was a chronic condition. The Panel considered that some lay people, particularly those who knew very little about schizophrenia, might assume that recovery meant elimination of the illness, particularly as the advertisement referred to a 'real chance' of recovery in the context of 'modern treatments' and described this as 'good news'. The advertisement was misleading in this regard. A breach of Clause 20.2 of the Code was ruled.

The Panel noted Janssen-Cilag's submission that the statement '… discuss with your doctor the choices available' encouraged patients to go to their doctors and discuss the treatment choices which might include psychosocial as well as pharmacological treatment

options. Whilst the advertisement referred to modern treatments there was no reference direct or implied to a specific medicine. There were several 'modern' treatment choices. The Panel did not consider that the statement at issue promoted a specific prescription only medicine to the public or would encourage patients to ask their health professional to prescribe a specific prescription only medicine. No breach of Clauses 20.1 and 20.2 was ruled.

The Panel noted that throughout the website certain terms were underlined. These links led to a glossary where an explanation was given. Underlined terms included 'psychiatrist', 'diagnosis' and 'mental health team'. In a section headed 'Newer medications' the phrase 'atypical antipsychotics' was underlined in a sentence which mentioned their mechanism of action and effect on a broader range of symptoms than older medications. The phrase 'long-acting injections' was underlined in the final sentence of the same section which listed the various presentations available. The reference to short-acting injections was not underlined. 'Long-acting injections' was also underlined in the preceding paragraph which dealt with older medications. The Panel noted that Janssen-Cilag's product, Risperdal Consta was the only atypical available as a long-acting injection. Given the format of the site wherein various terms were underlined throughout, the Panel did not consider that the underlining of the phrases at issue was inappropriate. It did not give them undue emphasis such that they either promoted a prescription only medicine to the general public or that encouraged members of the public to ask for a specific medicine, as alleged. No breach of Clauses 20.1 and 20.2 was ruled.

The Panel noted that one of the 'Ten Tips to Help you Discuss Treatment with your Doctor' was 'Ask your doctor if any of the newer treatments for schizophrenia would be suitable for you especially if you have had distressing side effects with other treatments'. The side effect section which appeared earlier in the website explained that the risk of certain side effects associated with newer medicines was much lower but not totally absent. The newer treatments were more likely to make people put on weight or have difficulty with sexual arousal. The Panel did not consider the bullet point at issue inferred that atypical antipsychotics were benign and thus superior to older medication as alleged. The website made it clear that side effects were associated with the newer medicines. No breach of Clause 20.2 was ruled.

The Panel did not consider that the description of schizophrenia as a 'disease of the mind' and references to abnormalities in the transfer and processing of information within the brain were unacceptable as alleged. The section 'Possible causes of Schizophrenia' explained that for the majority of people treatment relied on medicines which modified the effects of the neurotransmitters in the brain. It was also clearly stated that there was no known single cause of schizophrenia. The Panel did not consider that the phrase a 'disease of the mind' was unacceptable as alleged. No breach of Clause 20.2 was ruled.

The section 'The effect of discontinuing treatment' included the claim 'Antipsychotic drugs reduce the risk of future illness in patients who have recovered from an acute episode'. The claim did not refer to 'further illness' as stated by the complainant. The Panel did not consider that the claim as published on the website was a blatant lie as alleged. The effect of discontinuation of treatment and relapse rates were discussed. It was made clear that even with continued treatment patients might relapse. No breach of Clause 20.2 was ruled.

The Panel noted that the Brainchip link on the website featured an image of a man's face with a computer chip on his forehead. The link led to a self-help book for people experiencing psychosis, 'The Secret of the Brain Chip', which described a young man's experience of psychosis during which he felt that he was being controlled by a chip implanted in his brain. The booklet was produced with support from Janssen-Cilag. The booklet discussed treatment but did not mention a specific medicine or class of products. The Panel did not consider that it was an attempt to condition schizophrenic patients to the possibility of neuroleptics being delivered straight to the brain by surgical implant as alleged. The computer chip in the cartoon was depicted as a negative aspect of the patient's delusion rather than as part of the solution. No breach of Clauses 20.1 and 20.2 was ruled.

In considering the campaign as a whole the Panel noted that although no statements had been made to encourage a member of the public to ask for a specific prescription only medicine, the material was biased towards atypical antipsychotics ie the newer more modern treatments for schizophrenia. There were however, several atypical agents available. Nonetheless the Panel had some concerns about the bullet point 'Ask your doctor if any of the newer treatments for schizophrenia would be suitable for you especially if you have had distressing side effects with other treatments'. Whilst the atypical antipsychotics might be a rational treatment choice for newly diagnosed patients or those unable to tolerate the older agents, some patients would be satisfactorily controlled on their current treatment such that it would not be prudent to switch them to atypicals and risk a loss of control in the process. The bullet point seemed to open up that possibility to the patient although the final decision would always lie with the prescriber. Although noting its concerns the Panel, however, did not consider that either the advertisement or the website had failed to maintain a high standard; no breach of Clause 9.1 was ruled. Consequently the Panel also ruled no breach of Clause 2.

Complaint received 15 January 2007

Case completed 21 March 2007

CASE AUTH/1943/1/07

PRIMARY CARE TRUST PRESCRIBING HEAD v ASTRAZENECA

Meeting invitation

The head of prescribing at a primary care trust (PCT) complained about an invitation sent by AstraZeneca inviting delegates to a meeting about the future statin strategy for a local strategic health authority (SHA). The front page included the statement 'Sponsored by an educational grant from AstraZeneca'.

The complainant noted that the front page twice referred to the local SHA, however this meeting was not organised or in any way connected to the SHA.

The complainant noted that the terms and conditions on the back page seemed to make it clearer that the meeting was arranged entirely by AstraZeneca but he alleged that the layout of the document was misleading. It appeared from the front page that the local SHA was operating the meeting with support and sponsorship from AstraZeneca.

The Panel noted that AstraZeneca designed the meeting specifically to address the needs of the local SHA in the light of the recently issued Department of Health (DoH) statin agenda. It was thus not unreasonable to refer to the SHA in the title and description of the meeting. The only logo used on page 1 of the invitation, and anywhere else in the invitation, was AstraZeneca's. From the front page some readers might assume that AstraZeneca had sponsored a meeting on behalf of the SHA. This was not so. The meeting was solely under the direction of AstraZeneca. The Panel considered that the layout and content of the front page did not give clear information about AstraZeneca's role. In that regard high standards had not been maintained and a breach of the Code was ruled.

The Panel did not know the house style of SHA but it had not been given any reason to believe that the general layout of the invitation, particularly that of the front page, imitated the style used by the SHA. The registration form had to be returned to AstraZeneca. The Panel considered that the document might have been clearer but noting its ruling above decided that it was not in breach of the Code and ruled accordingly. It was clear that the meeting was sponsored by AstraZeneca. No breach of the Code was ruled.

The head of prescribing at a primary care trust (PCT) complained about a four page invitation sent by AstraZeneca inviting delegates to a meeting about the future statin strategy for a strategic health authority (SHA). Page 1 (the front cover of the invitation) stated the title of the meeting and gave a brief description of its purpose as follows:

> 'A cost-effective statin strategy for the [local] SHA
>
> Practical implementation of the DoH [Department of Health] statin agenda
>
> A practical and interactive meeting for clinicians and managers looking at implications and implementation of the changing statin agenda in the [local] SHA'

The date and venue were then stated and in the bottom left-hand corner of the page was the statement 'Sponsored by an educational grant from AstraZeneca'. The company name was in logo type and incorporated the strapline 'Cardiovascular bringing research to life'.

COMPLAINT

The complainant noted that page 1 of the invitation twice referred to the SHA, however investigations had shown that this meeting was not organised or in any way connected to that organisation. The complainant had originally been surprised that this relatively new organisation was quick to arrange such an event and obtain industry sponsorship, hence his curiosity about the meeting in the first place.

The complainant noted that the terms and conditions on the back page seemed to make it clearer that the meeting was arranged entirely by AstraZeneca but he alleged that the layout of the document was misleading. It appeared from the front page that the SHA was operating the meeting with support and sponsorship from AstraZeneca.

The complainant decided not to attend the meeting based upon this confusion and was also concerned that, from the invitation, the meeting appeared to be educational but might not actually be so on the day.

RESPONSE

AstraZeneca explained that the DoH recently sent a vascular pack to the SHAs providing recommendations on statin prescribing. During discussions with the chief executives of several SHAs, some suggested additional support in implementation of the recommendations would help to ensure safe and cost-effective prescribing within their regions. AstraZeneca submitted that these discussions had identified the need for this educational agenda within the re-structured organisations of the NHS. Specifically, the chief executive of the SHA and a professor from the DoH, welcomed AstraZeneca's support in this regard.

AstraZeneca noted that the four page invitation was professionally printed, the content of which was as follows:

- Page 1 – stated the title, venue, date with the AstraZeneca logo and sponsorship declaration
- Page 2 – provided the agenda for the educational meeting, including timings, titles of individual talks, speaker names, role and organisation
- Page 3 – summarised the background and purpose of the meeting
- Page 4 – provided AstraZeneca terms and conditions and registration form

AstraZeneca submitted that the information given on page 1 showed that the meeting had been designed to meet the needs of clinicians at a regional level, reflecting both the agenda of the SHA and of the DoH, regarding the use of statins. Both references to the SHA were appropriate, not misleading and not disparaging. A sponsorship declaration and the AstraZeneca logo were prominently displayed on page 1 of the invitation, as well as elsewhere, as required by Clause 19.3.

The meeting was not organised by the SHA. AstraZeneca noted that the main heading stated *for* the SHA and the subheading stated in the SHA. The language did not indicate any connection, endorsement from or joint organisational responsibilities with the SHA or its committees. Neither the SHA logo, nor the DoH logo was displayed on the front page, or elsewhere in the invitation. The only logo used was AstraZeneca's. The speakers and their presentations would address SHA specific issues which was why the name of the SHA appeared in the title.

AstraZeneca noted that although the complainant was surprised at the efficiency with which the meeting was organised he appeared not to question the validity, appropriateness or the standard of the proposed educational agenda.

AstraZeneca did not consider that the layout of the invitation was misleading. This was a straightforward four-page item. Each page carried the appropriate information to enable the recipient to decide whether they wished to attend the meeting. It was clear from the front page that the meeting was sponsored by AstraZeneca. It was appropriate to print the terms and conditions and registration form for the meeting on the back page.

AstraZeneca further noted that the complainant had acknowledged the educational content of the planned meeting. Indeed, the timings, speakers and their individual topics, as well as the organisations with which they were affiliated, had all been clearly indicated on page 2 of the invitation. The basis for the complainant's comment that the meeting might not be educational on the day was not clear, given the type of speakers and their background.

AstraZeneca acknowledged that the sponsorship statement on the front page of the invitation was used in error and should have stated 'Sponsored by AstraZeneca'. However, AstraZeneca submitted that the overall impression of the invitation was that this was clearly a meeting organised by AstraZeneca; no-one who completed the reply form would be in any doubt of that. Therefore, AstraZeneca submitted that there had been no breach of either Clause 19.3 or 7.2.

AstraZeneca further submitted that high standards had been maintained with no breach of either Clause 9.1 or 9.2. In addition, the meeting, which provided educational content and a forum for discussion relevant at a regional level, reflected the company's recognition of the recent organisational changes within the NHS and its desire to support its NHS customers by providing quality education.

PANEL RULING

The Panel noted that AstraZeneca designed the meeting specifically to address the needs of the SHA in the light of the recently issued DoH statin agenda. It was thus not unreasonable to refer to the SHA in the title and description of the meeting. The only logo used on page 1 of the invitation, and anywhere else in the invitation, was AstraZeneca's. From the front page some readers might assume that AstraZeneca had sponsored a meeting on behalf of the SHA. This was not so. The meeting was solely under the direction of AstraZeneca. The Panel considered that the layout and content of the front page did not give clear information about AstraZeneca's role. In that regard high standards had not been maintained and a breach of Clause 9.1 of the Code was ruled.

The Panel did not know the house style for the SHA's documents but it had not been given any reason to believe that the general layout of the invitation, particularly that of page 1, imitated the style used by the SHA. The registration form had to be returned to AstraZeneca. The Panel considered that the document might have been clearer but noting its ruling above decided that it was not in breach of Clause 7.2 of the Code and ruled accordingly. It was clear that the meeting was sponsored by AstraZeneca. No breach of Clause 19.3 was ruled.

The Panel did not consider that a ruling of a breach of Clause 2, which was reserved as a sign of particular censure, was warranted.

Complaint received 17 January 2007

Case completed 8 March 2007

CASE AUTH/1944/1/07

DRUG AND THERAPEUTICS BULLETIN/DIRECTOR v PFIZER

Promotion of Exubera

An article entitled 'Exubera: inhaled insulin for diabetes' which appeared in Drug and Therapeutics Bulletin (DTB), January 2007, criticised the promotion of Exubera (inhaled insulin human) by Pfizer. In accordance with established practice the matter was taken up by the Director as a complaint under the Code.

Exubera was indicated for the treatment of adults with type 2 diabetes mellitus not adequately controlled with oral antidiabetic agents and requiring insulin therapy. It was also indicated for the treatment of adults with type 1 diabetes mellitus, in addition to long or intermediate acting subcutaneous insulin, for whom the potential benefits of adding inhaled insulin outweighed the potential safety concerns.

The DTB article stated that despite the promotional claim that Exubera maintained 'long-term glycaemic control', experience of use in routine long-term management of diabetes was limited. The longer-term effects of continual exposure to high levels of insulin powder on the lungs were not known.

The Panel noted that the National Institute for Health and Clinical Excellence (NICE) technology appraisal for inhaled insulins stated that current guidelines recommended a target HbA1c of 6.5-7.5% although it was acknowledged that such targets might not be achieved in all patients. The NICE technology appraisal also stated that treatment with inhaled insulin should only be continued beyond 6 months and in the longer term if there was evidence of a sustained improvement in HbA1c that was judged to be clinically relevant to the individual patient's overall risk of developing long-term complications of diabetes.

Exubera was a new product and its summary of product characteristics (SPC) did not place any limit on the length of treatment with the product.

The Exubera European Public Assessment Report (EPAR) referred to studies that looked at HbA1c referring to HbA1c <8% as acceptable and HbA1c <7% as good.

The Panel noted that no claim relating to routine long-term management of diabetes was made. Claims for 'long-term glycaemic control' were made in various items. Skyler (2004) was cited to support the claims. Skyler (2004) compared the efficacy and safety of a regimen including inhaled insulin with conventional treatment in type 1 and type 2 diabetes over at least two years. The comparator arm was discontinued after two years due to the small number of patients (n=45). Of the 159 patients electing to continue on inhaled insulin 89 patients recorded at least four years of treatment. The mean HbA1c was 8.23% ± 1.21% after 4 years compared with 8.71% ± 1.49% at the start of treatment with inhaled insulin. A graph separated the results for type 1 and type 2 patients on inhaled insulins. Type 2 diabetics (n=57) had a mean HbA1c of around 9% which fell on commencement of treatment to around 7.7% gradually rising to around 8% after 4 years. Type 1 diabetics (n=31) had a mean HbA1c of around 8% which fell to around 7.5% gradually rising to around 8.5%. After 4 years the rate of overall hypoglycaemia decreased in the inhaled insulin group as did the rate of severe hypoglycaemia compared to the rates after 4 weeks of inhaled insulin treatment.

Jovanovic *et al* was a two year study in type 1 diabetics comparing subcutaneous and inhaled insulin. HbA1c started at 7.4% and rose to 7.5% (n=291) for the inhaled insulin group whereas levels fell in the subcutaneous group (7.5% to 7.3%) (n=291). Hypoglycaemic events per patient were essentially comparable in both groups. Severe hypoglycaemic events rates were lower with inhaled insulin, fasting plasma glucose (FPG) declined from 170.1 to 156.8mg/dL with inhaled insulin but rose with subcutaneous insulin (166.9 to 173.5mg/dL) and there was less weight gain with inhaled insulin.

Rosenstock *et al* was a two year study in type 2 diabetics comparing subcutaneous and inhaled insulin. HbA1c started at 7.7% and ended at 7.3% (n=319) for the inhaled insulin group and similarly fell in the subcutaneous group 7.8% to 7.3% (n=316). There were fewer hypoglycaemic events per patient with inhaled insulin. Severe hypoglycaemia event rates were comparable. There were greater FPG reductions (151.2 to 135.6mg/dL) with inhaled insulin than with subcutaneous insulin (148.2 to 147.1mg/dL) and less weight gain with inhaled insulin.

On balance the Panel considered that the two year data, Jovanovic *et al* and Rosenstock *et al*, showed that glycaemic control was maintained; HbA1c levels were similar to current guideline recommendations. Other studies over six months Quattrin *et al*, Skyler *et al* (2005) and Hollander *et al* concluded that inhaled insulin provided glycaemic control comparable to that with a conventional insulin regimen in both type 1 and type 2 diabetics.

The Panel considered that an important factor was the meaning of 'long-term'. In that regard, given the nature of diabetes the Panel did not accept that 6

month data was long enough and so in support of the claims at issue the results of Quattrin *et al*, Skyler et al (2005) and Hollander *et al* were disregarded. With regard to the remaining data the Panel considered that although Skyler (2004) followed patients for four years, patient numbers were very small (31 type 1 diabetics and 57 type 2 diabetics). The Skyler data suggested that after an initial dip in HbA1c levels following the initiation of inhaled insulin, levels rose over time. The more robust studies (Jovanovic *et al* and Rosenstock *et al*) were conducted over two years. The data appeared to show that glycaemic control with inhaled insulin was better in type 2 diabetes than in type 1 although the Panel noted that none of the papers reported statistical significance for any results. Both Skyler (2004) and Jovanovic *et al* reported increases in HbA1c over the course of their studies in type 1 diabetes although the clinical significance of the rise was not stated. Conversely Skyler (2004) and Rosenstock *et al* showed decreases from baseline HbA1c in type 2 diabetics. All studies reported positive results for inhaled insulin with regard to hypoglycaemia/severe hypoglycaemia event rates.

Beneath the heading 'Exubera – maintains long-term glycaemic control', in a detail aid, the data from Skyler (2004) appeared showing the results for type 1 and type 2 diabetes. The Panel considered the claim in the context of the graph. The Panel noted its comments on Skyler (2004) above. The data did not adequately demonstrate that glycaemic control had been maintained. The Panel considered the claim in association with the graph was misleading and not capable of substantiation. Breaches of the Code were ruled.

The detail aid included the claim 'Exubera – insulin to maintain long-term glycaemic control' referenced to Skyler (2004). No details from the study were given with the claim. The Panel did not consider that the Skyler (2004) data on its own was sufficient to substantiate the claim. It was thus misleading to cite Skyler (2004) in this regard and a breach of the Code was ruled. The Panel then considered whether the two year data supported the claim. The Panel noted its comment above regarding the two year data and considered that although there was data to show glycaemic control for two years in both type 1 and type 2 diabetes there appeared to be a possible difference in response between the two. The claim gave no indication of the time period and thus the Panel considered that, taking into account the two year data the unqualified claim was misleading and not capable of substantiation. The Panel ruled breaches of the Code.

Similar rulings were made in relation to advertisements which included the claim 'New Exubera…' 'Maintains long-term glycaemic control' referenced to Skyler (2004) and in relation to a slide set and two mailings.

An article entitled 'Exubera: inhaled insulin for diabetes' which appeared in the Drug and Therapeutics Bulletin (DTB), January 2007, criticised the promotion of Exubera (inhaled insulin human) by Pfizer Limited. In accordance with established practice the matter was taken up by the Director as a complaint under the Code.

Exubera was indicated for the treatment of adults with type 2 diabetes mellitus not adequately controlled with oral antidiabetic agents and requiring insulin therapy. It was also indicated for the treatment of adults with type 1 diabetes mellitus, in addition to long or intermediate acting subcutaneous insulin, for whom the potential benefits of adding inhaled insulin outweighed the potential safety concerns.

COMPLAINT

The DTB article stated that despite the promotional claim that Exubera maintained 'long-term glycaemic control', experience of use in routine long-term management of diabetes was limited. The longer-term effects of continual exposure to high levels of insulin powder on the lungs were not known.

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

RESPONSE

Pfizer submitted that as Exubera was a new product its use in routine, long-term management of diabetes was limited. Although there were limited data in routine use, there was data supporting long-term glycaemic control. However, there was no claim that Exubera should be used 'routinely'. Clearly the place of Exubera in the individual patient was a clinical decision based on the specific circumstances of the patient. Since its launch, the promotional materials had highlighted to health professionals that Exubera was a new product through the use of language, such as 'new' and 'introducing inhaled insulin' and use of the black triangle. The claim 'Exubera – Maintains long-term glycaemic control' was not synonymous with claiming that Exubera had been used in routine long-term management of diabetes.

Pfizer provided a number of publications that it submitted gave an up-to-date evaluation of the evidence in relation to Exubera and long-term control of HbA1c (six month, two year and four year data):

- Skyler (2004) looked at sustained long-term efficacy and safety of inhaled insulin during 4 years of continuous therapy.

- Jovanovic *et al* (2006) showed sustained efficacy and that inhaled insulin was well tolerated over a 2-year period in patients with type 1 diabetes.

- Rosenstock *et al* (2006) showed sustained efficacy and that inhaled insulin was well tolerated over a 2-year period in patients with type 2 diabetes.

- Quattrin *et al* (2004) compared the efficacy and safety of inhaled insulin with subcutaneous insulin

therapy in patients with type 1 diabetes in a 6-month, randomized, comparative trial.

- Skyler *et al* (2005) looked at the use of inhaled insulin in a basal/bolus insulin regimen in type 1 diabetic patients in a 6-month randomized, comparative trial.

- Hollander *et al* (2004) compared the efficacy and safety of inhaled insulin with subcutaneous insulin therapy in patients with type 2 diabetes in a 6-month, randomized, comparative trial.

Pfizer listed the most recent promotional materials for Exubera containing the claim, 'Exubera – insulin to maintain long-term glycaemic control':

a) Sales aid (EXU608) and electronic version of sales aid (EXU759)

Pfizer submitted this was for use by its speciality field force – the diabetes care team. A page entitled 'Exubera – maintains long-term glycaemic control' was carefully set in context within the sales aid. The flow of information clearly set out indications and contraindications then outlined pharmacodynamic data and clinical efficacy data. Study descriptions were included. The page relating to long-term control of HbA1c with Exubera followed the clinical efficacy data and clearly described the study. The claim appeared twice more through the detail aid.

The electronic version of the sales aid contained the same information and layout as the hardcopy booklet and provided the representatives with an alternative format (other than additional information on dosing which was not relevant to the claim relating to long-term control).

The representatives utilised these two items during sales calls with health professionals. The diabetes care team primarily called on specialists who initiated insulin therapy in diabetes, consultant diabetologists.

b) Advertising

Pfizer submitted recent examples of advertising in healthcare publications: EXU852A (Northern Ireland Medical Review) and EXU854F and EXU853F (Hospital Doctor).

c) Slide set for health professionals (EXU592a2/b2)

Pfizer submitted that this was a comprehensive slide set on Exubera, containing detailed notes. The CD-ROM was distributed via diabetes care team primarily to consultant diabetologists. The representatives did not use/present these slides.

Data on long-term glycaemic control was included within the slide set following extensive information on indications and contraindications for the product and the clinical efficacy data, including primary and secondary endpoints. Within the notes section of the slide there was detailed information for the health professional on the design and results of the study.

d) Mailings to health professionals

Pfizer submitted that the most recent mailings had been sent to GPs and respiratory clinicians in November 2006, copies were provided of EXU772 (GP mailing) and EXU773 (respiratory clinicians mailing).

Pfizer submitted that the promotional materials for Exubera had been pre-vetted by the Medicines and Healthcare products Regulatory Agency (MHRA). From January 2006 to June 2006 all of the promotional materials for Exubera were submitted and reviewed by the MHRA. This included the sales aid, the slide set, advertisements, and mailings. These materials included the claim 'Exubera – maintains long-term glycaemic control'.

In summary, Pfizer submitted that statements made in relation to the use of Exubera in the maintenance of long-term control were supported by the date and had been subject to extensive regulatory review. Pfizer made no claim for 'routine' use of Exubera in diabetes management and it did not, therefore, consider there was a *prima facie* case.

PANEL RULING

The Panel noted that the National Institute for Health and Clinical Excellence (NICE) technology appraisal for inhaled insulins stated that current guidelines recommended a target HbA1c of 6.5-7.5% although it was acknowledged that such targets might not be achieved in all patients. The NICE technology appraisal also stated that treatment with inhaled insulin should only be continued beyond 6 months and in the longer term if there was evidence of a sustained improvement in HbA1c that was judged to be clinically relevant to the individual patient's overall risk of developing long-term complications of diabetes.

Exubera was a new product and its summary of product characteristics (SPC) did not place any limit on the length of treatment with the product.

The Exubera European Public Assessment Report (EPAR) referred to studies that looked at HbA1c referring to HbA1c <8% as acceptable and HbA1c <7% as good.

The Panel noted that no claim relating to routine long-term management of diabetes was made. Claims for 'long-term glycaemic control' were made in various items. Skyler (2004) was cited to support the claims. Skyler (2004) compared the efficacy and safety of a regimen including inhaled insulin with conventional treatment in type 1 and type 2 diabetes over at least two years. The comparator arm was discontinued after two years due to the small number of patients (n=45). Of the 159 patients electing to continue on inhaled insulin 89 patients recorded at least four years of treatment. The mean HbA1c was 8.23% ± 1.21% after 4 years compared with 8.71% ± 1.49% at the start of treatment with inhaled insulin. A graph separated the results for type 1 and type 2 patients on inhaled

insulins. Type 2 diabetics (n=57) had a mean HbA1c of around 9% which fell on commencement of treatment to around 7.7% gradually rising to around 8% after 4 years. Type 1 diabetics (n=31) had a mean HbA1c of around 8% which fell to around 7.5% gradually rising to around 8.5%. After 4 years the rate of overall hypoglycaemia decreased in the inhaled insulin group as did the rate of severe hypoglycaemia compared to the rates after 4 weeks of inhaled insulin treatment.

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On balance the Panel considered that the two year data, Jovanovic *et al* and Rosenstock *et al*, showed that glycaemic control was maintained; HbA1c levels were similar to current guideline recommendations.

Other studies over six months Quattrin *et al*, Skyler *et al* (2005) and Hollander *et al* concluded that inhaled insulin provided glycaemic control comparable to that with a conventional insulin regimen in both type 1 and type 2 diabetics.

The Panel considered that an important factor was the meaning of 'long-term'. In that regard, given the nature of diabetes the Panel did not accept that 6 month data was long enough and so in support of the claims at issue the results of Quattrin *et al*, Skyler *et al* (2005) and Hollander *et al* were disregarded. With regard to the remaining data the Panel considered that although Skyler (2004) followed patients for four years, patient numbers were very small (31 type 1 diabetics and 57 type 2 diabetics). The Skyler data suggested that after an initial dip in HbA1c levels following the initiation of inhaled insulin, levels rose over time. The more robust studies (Jovanovic *et al* and Rosenstock *et al*) were conducted over two years. The data appeared to show that glycaemic control with inhaled insulin was better in type 2 diabetes than in type 1 although the Panel noted that none of the papers reported statistical significance for any results. Both Skyler (2004) and Jovanovic *et al* reported increases in HbA1c over the course of their studies in type 1 diabetes although the clinical significance of the rise was not stated. Conversely Skyler (2004) and Rosenstock *et al* showed decreases from baseline HbA1c in type 2 diabetics. All studies reported positive results for inhaled insulin with regard to hypoglycaemia/severe hypoglycaemia event rates.

The Panel examined each type of promotional item separately.

a) Exubera sales aids

One page was headed 'Exubera – maintains long-term glycaemic control' beneath which the data from Skyler (2004) appeared showing the results for type 1 and type 2 diabetes. The Panel considered the claim in the context of the graph. The Panel noted its comments on Skyler (2004) above. The data did not adequately demonstrate that glycaemic control had been maintained.

The Panel considered the claim in association with the graph was misleading and not capable of substantiation. Breaches of Clauses 7.2 and 7.4 were ruled.

Two more pages of the detail aid included the claim 'Exubera – insulin to maintain long-term glycaemic control' referenced to Skyler (2004). No details from the study were given with the claim.

The Panel did not consider that the Skyler (2004) data on its own was sufficient to substantiate the claim. It was thus misleading to cite Skyler (2004) in this regard and a breach of Clause 7.2 was ruled.

The Panel then considered whether the two year data supported the claim. The Panel noted its comment above regarding the two year data and considered that although there was data to show glycaemic control for two years in both type 1 and type 2 diabetes there appeared to be a possible difference in response between the two. The claim gave no indication of the time period and thus the Panel considered that, taking into account the two year data the unqualified claim was misleading and not capable of substantiation. The Panel ruled breaches of Clauses 7.2 and 7.4.

b) Advertisements

The advertisements included the claim 'New Exubera…' 'Maintains long-term glycaemic control' referenced to Skyler 2004.

The Panel did not consider that Skyler (2004) on its own was sufficient to substantiate the claim. It was thus misleading to cite Skyler 2004 in this regard and a breach of Clause 7.2 was ruled.

The Panel then considered whether the two year data supported the claim. The Panel noted its comment above regarding the two year data and considered that although there was data to show glycaemic

control for two years in both type 1 and type 2 diabetes there appeared to be a possible difference in response between the two. The claim gave no indication of the time period and thus the Panel considered that, taking into account the two year data the unqualified claim was misleading and not capable of substantiation. The Panel ruled breaches of Clauses 7.2 and 7.4.

c) Slide set

One slide was headed 'Long-term glycaemic control maintained- 4-year data' beneath which the data from Skyler (2004) appeared. The Panel considered its rulings in (a) above applied here.

d) Mailings

Both mailings included the claim 'Exubera is an insulin to maintain long-term glycaemic control' referenced to Skyler (2004). The Panel considered its rulings in (b) above applied here.

Complaint received **17 January 2007**

Case completed **5 March 2007**

CASE AUTH/1945/1/07

VOLUNTARY ADMISSION BY NOVARTIS

Promotion prior to grant of marketing authorization

Novartis voluntarily advised the Authority that an advertisement for amlodipine/valsartan (Exforge) currently in development, which appeared in Hospital Doctor and Doctor on 9 and 11 January, was in breach of the Code. Whilst the product had received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP), a UK marketing authorization had not been granted at the time.

Novartis reassured the Authority that the advertisement was not placed by the UK company, nor was it aware of its inclusion in the journals in question until after publication. Those responsible from Novartis' parent company in Basle had been reprimanded and reminded of the company's policies and of the UK company's commitment to comply with the Code. Steps had been taken to ensure that the advertisement would not reappear in UK journals.

Novartis apologised for the breach of the Code and reassured the Authority of its commitment to prevent any further occurrence.

The Director decided that as the matter related to the promotion of a medicine prior to the grant of its marketing authorization it was sufficiently serious for it to be taken up and dealt with as a complaint under the Code.

The Panel was very concerned at the publication of the advertisement given that the agency involved was said to have had extensive experience of publishing in the UK. The Panel noted that the advertisement promoted the amlodipine/valsartan combination prior to the grant of the UK marketing authorization for Exforge. Thus the Panel ruled a breach of the Code as acknowledged by Novartis.

The Panel noted the action taken by Novartis but considered that high standards had not been maintained. A further breach of the Code was ruled. On balance the Panel did not consider the circumstances warranted a ruling of a breach of Clause 2 of the Code which was used as a sign of particular censure.

Novartis Pharmaceuticals UK Ltd voluntarily advised the Authority that an advertisement feature which appeared in Hospital Doctor, 9 January 2007 and Doctor, 11 January was in breach of the Code.

COMPLAINT

Novartis noted that this feature included information on an amlodipine/valsartan combination (Exforge) currently in development by Novartis. Whilst this product had received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP), a UK marketing authorization had not been granted at the time.

Novartis reassured the Authority that this advertisement feature was not placed by the UK company, nor was it aware of its inclusion in the journals in question until after their publication. Those responsible from Novartis' parent company in Basle had been reprimanded and reminded of the company's policies and of the UK company's commitment to comply with the Code. Active steps had also been taken to ensure that this feature would not appear again in UK journals.

Novartis apologised that this breach of Clause 3.1 of the Code had arisen and reassured the Authority of its commitment to prevent any further occurrence.

The Director decided that as the matter related to the promotion of a medicine prior to the grant of its marketing authorization it was sufficiently serious for it to be taken up and dealt with as a complaint under the Code. Novartis was asked to respond in relation to Clauses 2, 3.1 and 9.1.

RESPONSE

Novartis submitted that Exforge received a UK marketing authorization on 17 January 2007. The UK company found out about the two advertisement features in question through someone telephoning its medical information department to ask about the licence status of the product. The UK company was not aware of the placement of the advertisement feature and instigated an urgent investigation to ascertain its origin and to prevent, if possible, its reappearance.

The advertisement came from an agency working on behalf of Novartis' parent company in Basle. It appeared that there had been basic errors within a team of individuals who should have been fully aware of Novartis' procedures and of the Code having had extensive experience of supporting the company and of publishing in the UK. The team involved had been severely reprimanded and reminded of Novartis' policies and of the seriousness of this breach of the Code. Following formal investigation by the agency, disciplinary action would be taken against those involved. Reassurances had also been sought from the agency of the steps that had been taken to ensure that no repetition of these events could occur.

Novartis apologised that these events had occurred and that despite the best efforts of the company both in

the UK and Basle it had been let down by an agency working on its behalf. As a result the UK company had been unknowingly involved in the promotion of a product ahead of the grant of the marketing authorization. Novartis accepted that this was a breach of Clause 3.1.

Novartis hoped however that the urgency with which this issue had been managed by the UK company and brought to the Authority's attention was some reassurance of the robustness of the UK company's procedures and its commitment to the Code.

Novartis advised that the Medicines and Healthcare products Regulatory Agency was also informed of these events on 17 January.

PANEL RULING

The Panel was very concerned at the publication of the advertisement given that the agency involved was said to have had extensive experience of publishing in the UK. The Panel noted that the advertisement feature promoted the amlodipine/valsartan combination prior to the grant of the UK marketing authorization for Exforge. Thus the Panel ruled a breach of Clause 3.1 of the Code as acknowledged by Novartis.

The Panel noted the action taken by Novartis but considered that high standards had not been maintained. A breach of Clause 9.1 of the Code was ruled. On balance the Panel did not consider the circumstances warranted a ruling of a breach of Clause 2 of the Code which was used as a sign of particular censure.

Proceedings commenced	**18 January 2007**
Case completed	**28 February 2007**

CASE AUTH/1946/1/07

PFIZER CONSUMER HEALTHCARE v Reckitt Benckiser Healthcare

'Quick Guide' on childhood fever

Pfizer Consumer Healthcare complained about a two page 'Quick Guide' article, 'Supported with an unrestricted educational grant from Reckitt Benckiser Healthcare', which appeared as a bound in insert in The Practitioner in November. The 'Quick Guide' was entitled 'Best practice in childhood fever – the comfort cycle' and referred to Nurofen for children (ibuprofen suspension) which was marketed by Reckitt Benckiser Healthcare.

Pfizer Consumer Healthcare's two key issues were the misleading and selective interpretation of the supporting data used and, more broadly speaking, the fact that this article was a promotional item as defined by the Code. The item was promotional because it incorporated a stylised image of the Nurofen for Children logo and the brand name appeared throughout the text. Furthermore Reckitt Benckiser Healthcare had effectively selected the subject matter by supplying specific data (including data on file) to the journal editors and had reviewed the copy prior to publication. Reckitt Benckiser Healthcare was thus able to influence the article in such a way as to favour its own interests. This article should thus be considered as an 'advertorial', covered by the Code, rather than an independently written best practice guide as implied by the statement 'supported with an unrestricted educational grant'. Overall, this article clearly appeared to have been written by or under the editorial control of Reckitt Benckiser Healthcare. Pfizer Consumer Healthcare alleged that the insert was misleading and constituted disguised promotion in breach of the Code.

The overall message, reinforced by the title, 'Best practice in childhood fever – the comfort cycle', was that Nurofen for Children represented best practice in treating childhood pain and fever. Several references to Nurofen for Children being 'treatment of choice' further strengthened this message. This was misleading and implied that the article was based on sound, accepted principles, preferably peer reviewed and supported by strong independently, published data. However two of the cited references were unpublished data on file and the third discussed anxiety in adolescents with chronic pain (Eccleston *et al* 2004). No link had been demonstrated between fever and anxiety in children or parents. Neither Nurofen for Children, nor indeed ibuprofen, was established as best practice in treating children's pain and/or fever. In fact a UK paediatric formulary recommended paracetamol as first line in fever. In conclusion both the title and contents misleadingly implied that they discussed genuine scientific opinion in breach of the Code.

The Dover study was one of the principal data on file references cited and was available on the Nurofen website. Pfizer Consumer Healthcare noted that this company sponsored randomised study compared the single dose efficacy and multiple dose tolerability of paracetamol with ibuprofen in paediatric fever. The single dose part of the trial was blinded while the second and subsequent doses were open-label. The primary endpoint of the study was the reduction of temperature from baseline at 6 hours following single dose administration of either paracetamol or ibuprofen. Secondary endpoints included subjective assessment of parent treatment preference.

Data from this study had been cherry picked to suit the 'Nurofen for Children Comfort Cycle' story that had been created in the article. The Dover study did not show a statistically significant difference between paracetamol and ibuprofen in reducing temperature (the primary endpoint). The article completely disregarded this less favourable primary endpoint and focussed instead on the more positive secondary endpoint of parent preference. Data extracted from this open-label element of the study was little more than market research. However it was presented in the article as fact and described as best practice in order to underpin and encourage confidence in the comfort cycle argument. There was no mention that this was a secondary endpoint or that it was open-label.

The open-label element of this study also meant that parents knew which medicine their child was to receive in subsequent dosing. This introduced significant bias into the study as parents were likely to be familiar with both medicines; it was likely that previous experience with taste, colour, brand recognition and dosing would influence their choice. This issue was discussed very briefly in the study but ignored in the article which unequivocally favoured Nurofen for Children over paracetamol. Despite this obvious source of bias the article recommended Nurofen for Children as the treatment of choice with parents *'which cannot be explained by product bias'*.

The comfort cycle was referenced specifically to the Dover study and implied that reducing parental anxiety reduced anxiety in children which in turn tackled fever. It did not appear that the study even assessed anxiety and, in fact, the study report described this speculative link as a 'working hypothesis'. This misinterpretation of the data breached the Code.

Eccleston *et al* was another study cited in support of the comfort cycle story but as it investigated a very

different patient group than that discussed in the article it could not be used as supporting evidence. Eccleston *et al* measured distress associated with *chronic pain* in *adolescents* and how they coped while the article at issue discussed anxiety associated with acute pain in children. Nurofen for Children was licensed to treat mild to moderate pain and fever in children up to the age of 12 years; it was not intended for long term use. Eccleston *et al* investigated adolescents (mean age 14.45 years). Pfizer Consumer Healthcare accepted that the lower end of this age range was 11 years and so within the Nurofen for Children's licence. However the article at issue did not refer to adolescents and implied that the published evidence used for their anxiety-pain hypothesis applied to a much younger age group.

Eccleston *et al* investigated anxiety relating to *chronic* pain and did not investigate a relationship between anxiety and acute pain. The article did not state that the supporting data referred specifically to chronic pain in adolescents. The article, without the benefit of further clinical evidence, then went on to extend on this anxiety/pain association by stating that it followed that anxiety must also result from fever as well, thus completing the comfort cycle. Though not specifically referenced beyond the initial anxiety-pain statement the citation of Eccleston *et al* added a degree of apparent credibility to the article. It was clear that this data had been misrepresented so that it fitted in with the comfort cycle story. Pfizer Consumer Healthcare alleged that it was inappropriate to cite this reference in an article that specifically discussed the use of a medicine for the treatment of acute pain in children.

In summary the concept of the comfort cycle formed the basis for the whole piece and had been presented as fact in order to influence prescribing decisions in childhood fever. However this was conjecture and based on a working hypothesis as discussed in the Dover study. Little or no factual data had been presented in support of the comfort cycle model.

Pfizer Consumer Healthcare noted that a bar chart at the top of the first page clearly implied that, at the end of the Dover study, more than twice as many parents would use Nurofen for Children again compared with paracetamol. In reality this difference was about 9%. This use of suppressed zeros was grossly misleading and was clearly and specifically prohibited in the Code.

The article described Nurofen for Children as '… achieving excellent analgesia (at least as good as paracetamol) …' which clearly implied superiority of Nurofen for Children over paracetamol. If the intention was to communicate parity then a statement to the effect of 'as good as paracetamol' would have been sufficient. As pain was not measured in any of the studies cited in the article at issue this statement was not substantiated, either in terms of being 'excellent' or in its comparison with paracetamol. The reference cited related to fever and not analgesia. Pfizer Consumer Healthcare alleged this unsubstantiated claim together with a misleading reference to an irrelevant study constituted a breach of the Code.

Pfizer Consumer Healthcare alleged further breaches of the Code in that the non-proprietary name was not adjacent to the most prominent display of the brand name, there was no statement on the first page of the advertorial as to where the prescribing information might be found, and nor was there information describing the adverse event reporting mechanism.

In summary the article was misleading in its overall message, presentation and interpretation of the data. It was branded and promotional but presented as an independently written 'best practice' article. The information had been presented as established scientific opinion, rather than a working hypothesis requiring further investigation, in such a way as to influence prescribing decisions in childhood fever.

The Panel had first to consider whether the 'Quick Guide' article was covered by the Code. Nurofen for Children was a product which, for childhood fever, the subject of the article in question, could be bought over-the-counter (OTC) or prescribed; sales data showed that most packs of Nurofen for Children were purchased OTC. The supplementary information stated that the Code did not apply to the promotion of OTC medicines to members of the health professions when the object of that promotion was to encourage their purchase by the public. Where an advertisement was designed to encourage doctors to prescribe the medicine, then it came within the scope of the Code. An item that promoted for both prescribing and recommending purchase would need to comply with both the ABPI Code and the PAGB Professional Code.

The 'Quick Guide' article referred to the comfort cycle and how important a parent's perception of therapy was in the management of a child's pain. The article stated that 'Prescribing or recommending a treatment of choice will ultimately benefit both [parent] and child'. The Panel acknowledged that although very few packs of Nurofen for Children were prescribed this was not a relevant factor in deciding whether the ABPI Code applied or not. The article referred to prescribing and thus would encourage some doctors to prescribe Nurofen for Children. The Panel considered that the 'Quick Guide' article fell within the scope of the Code.

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 interests. 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 article at issue was developed after Reckitt Benckiser Healthcare had contacted the publishers with a view to introducing GPs to, *inter alia*, the concept of the comfort cycle. Reckitt Benckiser Healthcare provided relevant information and was able to comment on the final article and had paid for it to be included in the journal; the production of the article had thus not been a strictly arm's length arrangement. The article featured, as part of the heading to both pages, a logo which incorporated the red/orange/yellow 'target' associated with the Nurofen brand. The Panel considered that this, together with the company's involvement in the development of the article, meant that Reckitt Benckiser Healthcare was responsible for its content under the Code.

At first glance the article appeared to be an educational discussion about how best to manage childhood fever; an impression strengthened by the statement that the insert had been 'Supported with an unrestricted educational grant from Reckitt Benckiser Healthcare'. The 'Quick Guide' had been provided as an insert in The Practitioner and was intended to be kept for future reference. The only treatments discussed in the article, however, were paracetamol and Nurofen for Children. The Panel noted the way in which the material had been developed; Reckitt Benckiser Healthcare was inextricably linked to the production of the insert. Given the company's involvement the Panel considered that the article was disguised promotional material for Nurofen for Children; the declaration of sponsorship implied that it was an independently written educational piece which was not so. A breach of the Code was ruled.

The Panel noted Pfizer Consumer Healthcare's submission that a UK paediatric formulary recommended paracetamol as first line in fever. The title of the article was 'Best practice in childhood fever – the comfort cycle' but the only treatments referred to were Nurofen for Children and paracetamol. It was stated that Nurofen for Children had emerged as a treatment of choice with parents. A diagram of 'The comfort cycle' featured 'Nurofen for Children' in the middle of a cycle of arrows; one arrow was labelled 'Becomes parent's treatment of choice'. The Panel considered that the diagram implied that Nurofen for Children became the treatment of choice for parents. The Panel further considered that as the article was principally about Nurofen for Children, the title 'Best practice in childhood fever – the comfort cycle' implied that Nurofen for Children had been clinically shown to represent best practice which was not so. The Panel considered that the overall message of the article was misleading as alleged. A breach of the Code was ruled.

Reckitt Benckiser Healthcare had not provided any information about the Dover Study other than that mentioned in its response. The diagram depicting 'The comfort cycle' was referenced to the Dover study and depicted a four stage cycle of 'Reduces anxiety in children', 'Tackles fever', 'Becomes parent's treatment of choice' and 'Reduces anxiety in parent' around 'Nurofen for Children' in the centre. The Panel considered that the diagram implied that because it tackled fever, Nurofen for Children became the parent's choice. A description of the study in the text stated that when compared with paracetamol suspension, parents rated Nurofen for Children as more efficacious. According to Pfizer Consumer Healthcare there was, however, no difference between the two medicines with regard to the primary clinical outcome of reduction in temperature/fever. The Panel also noted that the concept of the comfort cycle was a 'working hypothesis'. The Dover study had not measured anxiety in either the parents or the children. The Panel thus considered the article was misleading as it was not a fair reflection of the results of the Dover study. A breach of the Code was ruled.

Eccleston *et al*, cited in support of the statement 'Anxiety is a measure of pain…', reported on adolescent chronic pain, not childhood fever, the subject of the insert in question. The patients in Eccleston *et al* ranged from 11 to 17 years (mean 14.45 years) and the study examined emotional distress in adolescent chronic pain patients and their parents and the relationship between the two and adolescent coping. The Panel questioned the relevance of the study in the context of a piece about childhood fever which required only short-term treatment. There was no data to show that the relationship between anxiety and pain in adolescents with chronic pain was the same as in infants with acute pain or fever. Nurofen for Children was indicated for children from 3 months to 12 years of age. The Panel considered that citing Eccleston *et al* was misleading as alleged. A breach of the Code was ruled.

The y axis of the bar chart which depicted the percentage of parents who would use either Nurofen for Children or paracetamol again (as reported in the Dover study) started at 82%. The resultant height of the bars made it look as if twice as many parents preferred Nurofen for Children as preferred paracetamol which was not so. The Panel considered that the use of the suppressed zero was misleading in breach of the Code.

The Panel noted that on the available information the Dover Study had not measured analgesia. Reckitt Benckiser Healthcare Healthcare submitted that it was widely accepted that ibuprofen was at least as good as paracetamol and that the superiority of ibuprofen was capable of substantiation citing McGaw *et al* in this regard. The claim 'At least as good as paracetamol' was not referenced as such nor did the Code require it to be referenced. The Code did not require substantiation to be provided in the article itself but the claim must be capable of substantiation. The Panel considered that readers might assume that the Dover study measured pain/analgesia given that the article stated the data was presented at the International Symposium on Paediatric Pain.

McGaw *et al* compared ibuprofen with acetaminophen in the relief of postextraction dental pain in children aged 8 - 16 with the majority of the children in the 14 - 16 age range. The authors commented that postoperative pain associated with dental surgery was associated with pain and oedema and that ibuprofen's superior analgesic efficacy might be due in part to its anti-inflammatory properties which were not shared by acetaminophen. The Panel considered that in the circumstances the reference to 'excellent analgesia (at least as good as paracetamol)' was misleading and a breach of the Code was ruled.

The Panel considered that the most prominent display of the brand name was not accompanied by the non-proprietary name. A breach of the Code was ruled.

The 'Quick Guide' was provided as a bound-in insert in The Practitioner' it was thus a two page advertisement where the prescribing information appeared overleaf. There was, however, no statement as to where the prescribing information could be found. A breach of the Code was ruled.

The Code required that all promotional material, other than promotional aids, must include prominent information about adverse event reporting mechanisms. No such information was given in the 'Quick Guide' at issue. A breach of the Code was ruled.

Pfizer Consumer Healthcare complained about a 'Quick Guide' article, 'Supported with an unrestricted educational grant from Reckitt Benckiser Healthcare', which appeared as an insert in The Practitioner in November 2006. The subject of the 'Quick Guide' was 'Best practice in childhood fever – the comfort cycle'.

COMPLAINT

Pfizer Consumer Healthcare stated that its two key issues, from which further more specific concerns arose, were the misleading and selective interpretation of the supporting data used and, more broadly speaking, the fact that this article was a promotional item and fulfilled the Code's definition of such an item. Pfizer Consumer Healthcare believed the item was promotional because:

- it was clearly branded in the top right corner with a stylised image of the Nurofen for Children logo;
- the brand name Nurofen for Children (ibuprofen suspension) appeared throughout the text;
- Reckitt Benckiser Healthcare (UK) Limited had effectively selected the subject matter by supplying specific data (including data on file) to the journal editors – some of this subject matter such as the graph showing patient preference had been used in the article unaltered;
- Reckitt Benckiser Healthcare had reviewed the copy prior to publication.

It was clear that Reckitt Benckiser Healthcare was able to influence the article in such a way as to favour its own interests. This article should thus be considered as promotional and covered by the Code, rather than an independently written best practice guide as implied.

Disguised promotion

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 statement that Reckitt Benckiser Healthcare had provided an unrestricted educational grant to support the article, clearly implied that the item was independently produced. On closer inspection it was plain that there was significant company involvement. The article was heavily branded with numerous inclusions of the brand name, Nurofen for Children, as well as the prominent inclusion of a stylised version of the Nurofen 'target' logo at the top of the piece. This impression was reinforced by the fact that two out of the three supporting references were unpublished data on file and therefore not available without company permission.

With the inclusion of branding, prescribing information and the adherence to the two-page limit for journal advertisements, Pfizer Consumer Healthcare suggested that this article constituted an 'advertorial' rather than an independently produced editorial as the title and general style suggested.

Overall, this article clearly appeared to have been written by or under the editorial control of Reckitt Benckiser Healthcare. Pfizer Consumer Healthcare alleged that the insert was misleading and constituted disguised promotion in breach of Clause 10.1 of the Code.

Pfizer Consumer Healthcare queried who had authored this piece and in particular if any public relations or advertising agencies were involved.

The overall theme of the article

The overall message, reinforced by the title, 'Best practice in childhood fever – the comfort cycle', was that Nurofen for Children represented best practice in treating childhood pain and fever. In addition there were several references to Nurofen for Children being 'treatment of choice' which further strengthened this message.

This was misleading and implied that the article was based on sound, accepted principles, preferably peer reviewed and supported by strong independently, published data. However two of the cited references were unpublished data on file and the third discussed anxiety in *adolescents* with *chronic pain* (Eccleston *et al* 2004). Pfizer Consumer Healthcare also noted that no link had been demonstrated between fever and anxiety in children or parents. Neither Nurofen for Children, nor indeed ibuprofen, was established as best practice in treating children's pain and/or fever. In fact

'Medicines for Children' which was jointly published by the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists' Group recommended paracetamol as first line in fever.

In conclusion both the title and contents misleadingly implied that they discussed genuine scientific opinion in breach of Clause 7.2.

The 'comfort cycle'

The Dover study was one of the principal data on file references cited. Its methodology and results were available on the Nurofen website. Pfizer Consumer Healthcare noted that the objective of this company sponsored randomised study was to compare the single dose efficacy and multiple dose tolerability of paracetamol with ibuprofen in paediatric fever. The single dose part of the trial was blinded while the second and subsequent doses were open-label.

The primary endpoint of the Dover study was the reduction of temperature from baseline at 6 hours following single dose administration of either paracetamol or ibuprofen. Secondary endpoints included a number of measures including subjective assessment of parent treatment preference.

Data from this study had been cherry picked to suit the 'Nurofen for Children Comfort Cycle' story that had been created in the article. The Dover study did not demonstrate a statistically significant difference between paracetamol and ibuprofen in reducing temperature (the primary endpoint). The article completely disregarded this less favourable primary endpoint and focussed instead on the more positive secondary endpoint of parent preference. It was clear from this open-label element of the study that the data extracted was little more than market research. However it was presented in the article as fact and described as best practice in order to underpin and encourage confidence in the comfort cycle argument. There was no mention that this was only a secondary endpoint or that it was open-label.

The open-label element of this study also meant that parents were aware of which medicines their child was to receive in subsequent dosing. This introduced significant bias into the study as parents were likely to be familiar with both medicines; it was likely that previous experience with taste, colour, brand recognition and dosing would influence their choice. This issue was discussed very briefly in the study but ignored in the article which unequivocally favoured Nurofen for Children over paracetamol. Despite this obvious source of bias the article still recommended Nurofen for Children as the treatment of choice with parents *'which cannot be explained by product bias'*.

The comfort cycle was referenced specifically to the Dover study and implied that reducing parental anxiety reduced anxiety in children which in turn tackled fever. It did not appear that the study even assessed anxiety and, in fact, the study report described this speculative link as a 'working hypothesis'. Pfizer Consumer Healthcare alleged that this misinterpretation of the data was a breach of Clause 7.2.

Eccleston *et al* was another key study used to build up credibility and support for the comfort cycle story. However that paper investigated a very different patient group than that discussed anywhere in the article and so could not be used as supporting evidence. Eccleston *et al* measured the extent of distress associated with *chronic pain* in *adolescents* and how they coped while the article at issue discussed anxiety associated with acute pain in children.

Nurofen for Children was only licensed for children up to the age of 12 years. Eccleston *et al* investigated adolescents (mean age 14.45 years). Pfizer Consumer Healthcare accepted that the lower end of this age range was 11 years and so within the Nurofen for Children's licence. However the article at issue did not refer to adolescents and implied that the published evidence used for their anxiety-pain hypothesis applied to a much younger age group.

Nurofen for Children was an over-the-counter (OTC) medicine licensed to treat mild to moderate pain and fever; it was not intended for long term use. Eccleston *et al* investigated anxiety relating to *chronic* pain and did not investigate a relationship between anxiety and acute pain. The article did not state that the supporting data referred specifically to chronic pain in adolescents.

The article, without the benefit of further clinical evidence, then went on to extend on this anxiety/pain association by stating that it followed that anxiety must also result from fever as well, thus completing the comfort cycle.

Though not specifically referenced beyond the initial anxiety-pain statement the citation of Eccleston *et al* added a degree of apparent credibility to the article. It was clear that this data had been misrepresented so that it fitted in with the comfort cycle story. Pfizer Consumer Healthcare alleged that it was inappropriate to cite this reference in an article that specifically discussed the use of an OTC medicine for the treatment of acute pain in children, in breach of Clause 7.2.

In summary the concept of the comfort cycle formed the basis for the whole piece and had been presented as fact in order to influence prescribing decisions in childhood fever. However this was pure conjecture and based on a working hypothesis as discussed in the Dover study. Little or no factual data had been presented in support of the comfort cycle model.

Misrepresentation of data

Pfizer Consumer Healthcare noted that by the use of suppressed zero, a bar chart at the top of the first page clearly implied that, at the end of the Dover study, more than twice as many parents would use Nurofen for Children again compared with paracetamol. In reality this difference was about 9%. The use of a suppressed zero was misleading and clearly in breach of Clause 7.8.

Implied superiority without substantiation

The article described Nurofen for Children as '… achieving excellent analgesia (at least as good as paracetamol) …'. This clearly implied superiority of Nurofen for Children over paracetamol. If the intention was to communicate parity then a statement to the effect of 'as good as paracetamol' would have been sufficient. As pain was not measured in any of the studies cited in the article at issue this statement was not substantiated, either in terms of being 'excellent' or in its comparison with paracetamol. The reference cited related to fever and not analgesia. Pfizer Consumer Healthcare alleged this unsubstantiated comparative claim together with a misleading reference to an irrelevant study constituted a breach of Clause 7.2.

Clause 4 breaches

Pfizer Consumer Healthcare alleged that the following had been omitted.

- the non-proprietary name which must appear adjacent to the most prominent display of the brand name (breach Clause 4.6);
- a statement on the first page of the advertorial describing where the prescribing information might be found (breach Clause 4.7);
- a prominent display of information describing the adverse event reporting mechanism (breach Clause 4.10).

Summary

In summary the article was grossly misleading in its overall message, presentation and interpretation of the data. It was branded and promotional but presented as an independently written 'best practice' article. The information had been presented as established scientific opinion, rather than a working hypothesis requiring further investigation, in such a way as to influence prescribing decisions in childhood fever.

RESPONSE

Reckitt Benckiser Healthcare did not consider that this complaint was appropriate for consideration by the Authority because it related to an educational article concerning an OTC product; this particular piece was outside of the scope of the ABPI Code.

Clause 1.1 of the Code stated that the Code did not apply to the promotion of OTC medicines to members of the health professions when the object of that promotion was to encourage their purchase by members of the public. As indicated below, Reckitt Benckiser Healthcare did not consider that this publication was promotional, but even if it was, it was exempted by the final paragraph of Clause 1.1.

The 'Quick Guide' insert was published in The Practitioner, a journal targeted at, and circulated solely to UK GPs. However, if the article was considered to be promotional, Reckitt Benckiser Healthcare considered that it would encourage GPs to recommend Nurofen for Children to parents, for their later purchase, rather than prescription. A small number of GPs did prescribe Nurofen for Children, though it was principally an OTC product; the ratio of OTC sales to prescription sales was tiny, approximately 28:1. The design of the packaging was also clearly aimed at consumer sales, rather than prescription, and was noticeably different from the majority of prescription medicines currently available, ie predominantly plain white packs. In other words, prescription accounted for a mere 3.5% of total UK sales of Nurofen for Children.

The last paragraph of column 2 of the article in question stated that 'Prescribing or recommending a treatment of choice will ultimately benefit both [parent] and child'. The word 'parent' was consistent with the theme of the article on the comfort cycle and allaying parental anxiety. The use of the word 'recommending' was also consistent with Reckitt Benckiser Healthcare's view of the intention of the article, and a single use of the word 'prescribing' was not of itself significant in the circumstances.

Reckitt Benckiser Healthcare explained that it had contacted the publishers of The Practitioner with a view to introducing GPs to the concepts of the comfort cycle and a bound-in insert in The Practitioner was agreed upon. Reckitt Benckiser Healthcare made an educational grant to assist in the cost of circulation. No agency was involved in the production of this item. The publishers generated the initial concept insert; Reckitt Benckiser Healthcare provided data and information on ibuprofen and the comfort cycle to assist in the writing of the article. Whilst Reckitt Benckiser Healthcare was able to comment on the finished manuscript, the editors of The Practitioner had final editorial control.

Reckitt Benckiser Healthcare provided the publishers with the essential information [prescribing information], as was required under the Proprietary Association of Great Britain (PAGB) Professional Code of Practice, as appeared in the final version of the insert. This was in the belief that this item was targeted at GPs and to be kept by the intended audience for their future reference and recommendation to parents for purchase.

As stated above, a single paragraph in the insert included the word 'prescribing'. This was the author's choice and Reckitt Benckiser Healthcare did not have editorial control over the article.

Alleged disguised promotion

Reckitt Benckiser Healthcare noted that Clause 10.1 of the Code stated that promotional material and activities must not be disguised.

As stated prominently on the item, Reckitt Benckiser Healthcare had provided an unrestricted educational grant in order to make the publication and circulation of this important information possible. Thus the requirements of Clause 10.1 and, indeed, Clause 9.10,

of the Code had been met.

Notwithstanding this, Reckitt Benckiser Healthcare strongly believed that it would be wrong to suggest that the article constituted disguised promotion. Firstly, the article was not designed to be promotional in nature; it discussed the comfort cycle and communicated the results of the Dover study presented at the recent international symposium on paediatric pain (which utilised Nurofen for Children as a treatment arm).

Secondly, Reckitt Benckiser Healthcare's involvement was not disguised; there was a prominent statement at the top of the article, that the company had provided the educational grant to allow its circulation to GPs. If a company wished to disguise a piece of promotional material it would not have declared its financial interest to the readers so openly. Reckitt Benckiser Healthcare had made this declaration very clear to the reader, to allow them to make an informed judgment.

The brand name Nurofen for Children was used in the article as it was the product used as an active treatment arm in the Dover study.

The inclusion of the Nurofen logo, use of the brand name Nurofen for Children and the fact that Reckitt Benckiser Healthcare provided information for the insert and was able to comment on it prior to its publication, was immaterial, as these elements did not in themselves make the item promotional, whether disguised or not.

The use of data on file as supporting data was accepted practice in the pharmaceutical industry. Use of such data meant that Reckitt Benckiser Healthcare was required to provide it on request to health professionals or appropriate administrative staff. In contrast to Pfizer Consumer Healthcare's allegation, this did not mean that it was not available without Reckitt Benckiser Healthcare's permission.

Reckitt Benckiser Healthcare therefore contested the allegation that the article was in breach of Clause 10.1; it did not consider it to be promotional in nature, disguised or otherwise.

Overall theme of the article

Reckitt Benckiser Healthcare noted that Pfizer Consumer Healthcare took issue with the overall theme of the insert. In particular, Pfizer Consumer Healthcare appeared to believe that the insert represented the use of ibuprofen as best practice in treating childhood pain and fever, and that Nurofen for Children was emerging as a treatment of choice with parents. This was wrong; the best practice referred to, even within the title, was to the comfort cycle and not ibuprofen suspension.

With regard to a treatment of choice the authors had carefully chosen the indefinite article 'a' rather than the definite article 'the' when referring to 'treatment of choice'. The insert did not claim Nurofen for Children to be 'the' treatment of choice with parents, but merely 'a' treatment of choice with parents. This careful selection of wording presumably resulted from a thorough reading and understanding of the Dover study. Reckitt Benckiser Healthcare noted that the complaint studiously avoided the use of any definite article when referring to treatment of choice.

Reckitt Benckiser Healthcare also noted that, within the text of the insert, this parental preference was repeatedly referred to as a treatment of choice with parents, rather than for parents or, for that matter, physicians.

Whilst some professional health organisations might have recommended paracetamol as the first line treatment in fever, the Dover study had shown in its secondary endpoint that Nurofen for Children could be 'a' treatment of choice for parents, in that 96.7% of parents had stated that they would use Nurofen for Children again, compared with 87.9% who would use paracetamol again ($p < 0.01$).

Recommendation of a treatment that, in addition to treating the child was also the preferred choice of the parent, was likely to allay parental anxiety, and was thus a clear link to the comfort cycle. Moreover, the reason that Nurofen for Children was specifically referred to in the insert was because it was used in the Dover study. Reckitt Benckiser Healthcare considered that this parental preference was accurately and fairly represented as 'a' treatment of choice, and that the Dover study, being a very recent piece of work, represented an up-to-date evaluation.

Reckitt Benckiser Healthcare noted that Pfizer Consumer Healthcare had objected to the fact that parts, and not all, of the Dover study end points and results were presented. Reckitt Benckiser Healthcare submitted that it was standard practice by clinical investigators to publish findings of a large study in separate sections, in different journals, at different times. The Dover study was a large study with many findings. The results of the primary efficacy and safety end points had been submitted to a reputable journal and the manuscript was currently undergoing peer-review. The results of comparative efficacy between ibuprofen and paracetamol were also the subject of current peer-review. For reasons of confidentiality as well as observing the Code with regard to peer-review, Reckitt Benckiser Healthcare could not currently discuss the details of the primary end points. Added to this was the fact that word-count limitations were often set by journals, so it was not always possible to include discussion of all findings in the primary manuscript when submitted for publication. However, sufficient details of the study had been made publicly available on Reckitt Benckiser Healthcare's website which Pfizer Consumer Healthcare had downloaded and included in its complaint. This demonstrated the open approach taken by Reckitt Benckiser Healthcare in communicating these study results.

In view of these various facets, secondary end points were often discussed in a journal different to the one in which the primary manuscript was published. Selecting the particular secondary end point of parental preference was most appropriate here, given that the

insert was intended to give that much more focus to this very issue, and to a tightly targeted audience.

Reckitt Benckiser Healthcare submitted that selecting secondary end points in such a publication was an accepted practice; as there was no bias in the presentation of this secondary end point, there was no breach of any specific clause of the Code, or its spirit.

With regard to concerns raised by Pfizer Consumer Healthcare over the phrase 'which cannot be explained by product bias', Reckitt Benckiser Healthcare believed that this was a fair, balanced, undistorted portrayal of the interpretation made by the authors of the trial report.

Although the parents' perception of efficacy was a subjective criterion, the randomised, double blind, double dummy nature of the study meant that parental preference would be equally split between the two groups, and that the significant difference between treatment groups was most probably as a result of better resolution of all associated symptoms, rather than bias as suggested by Pfizer Consumer Healthcare.

Parental preference was already evident at the end of the randomised, double blind, double dummy element of the study, and continued into the second, open element. In contrast, had this been a fully open-label study, Pfizer Consumer Healthcare's criticism might have been valid.

It was acknowledged that the second part of this study was conducted as an open study: parents knew whether their child was taking paracetamol or Nurofen for Children. This 'product bias' was hence known to all parents involved. Yet the level of preference expressed at the end of the study when compared to that expressed after the first phase did not differ to any great degree. After initial dose (the randomised, double blind phase of the study), 96.5% (138/143) of parents said they would use ibuprofen again, compared to 88.8% (127/143) of the paracetamol group ($p < 0.05$). At end of treatment (at the end of open phase of the study), 96.7% (145/150) of parents said they would use ibuprofen again, compared to 87.9% (131/149) in the paracetamol group ($p < 0.01$). After initial dose, 59.2% (87/147) of parents graded ibuprofen as very efficacious, compared to 37.2% (55/148) of the paracetamol group ($p < 0.001$). At end of treatment, 59.6% (90/151) of parents graded ibuprofen as very efficacious, compared to 43.3% (65/150) in the paracetamol group ($p < 0.01$).

The fact that parents whose children were taking Nurofen for Children preferred it to a greater extent than the preference expressed for paracetamol by parents whose children were taking that product, indisputably showed that 'product bias' was not the only factor affecting parental choice.

Hence the conclusion 'which cannot be explained by product bias' was indeed accurate. All data on parental preference were accurately reflected in the text, and described correctly so as not to mislead the reader. If Pfizer Consumer Healthcare wished to contest the interpretation of the data, it should write to the investigators of the Dover study. Interpretation of the study findings was independent from Reckitt Benckiser Healthcare; it was important for all parties to respect this independence. Additionally, the accusation that this was little more than market research data was unacceptable and constituted denigration of the academic work by the investigators of the Dover study.

With regard to alleged inappropriate referencing, Reckitt Benckiser Healthcare noted that Eccleston *et al* was not cited in support of a promotional claim, but merely to explain that anxiety was a measure of pain. This was a well-conducted study using a large number of sophisticated psychological instruments to measure the emotional status of young patients and their parents. Study of anxiety with acute pain was difficult, given the short-term and relatively transient nature of acute pain; hence this study had taken chronic pain as a study model. It included children aged 11 to 17, and provided a reasonable surrogate for children younger than 12 (the upper age limit for which Nurofen for Children was licensed), who could have practical difficulties in participating in anxiety assessment. Reckitt Benckiser Healthcare believed that it provided a sound scientific basis for the discussion on the complex area of anxiety and pain, and was both objective and fair.

When considering all of the above, Reckitt Benckiser Healthcare believed that it had demonstrated that the article in question did not mislead and did not distort or exaggerate. The company thus denied a breach of Clause 7.2.

Alleged misrepresentation of data

Reckitt Benckiser Healthcare acknowledged that the bar chart had a suppressed zero on the y-axis, but reiterated that the article was written by the editor of The Practitioner, primarily as an educational piece, and did not fall within the scope of the Code. There was thus no breach of Clause 7.8.

Where Reckitt Benckiser Healthcare did have editorial control, it would of course take the use of suppressed zeros into account and ensure that information was clearly represented in educational and scientific material produced by it.

Alleged implied superiority without substantiation

It was widely accepted clinically that ibuprofen was at least as good as paracetamol. As no claim of superiority was made in this piece, the authors undoubtedly considered that it was thus unnecessary to elaborate further on this point. This was despite the fact that superiority of ibuprofen was capable of substantiation (McGaw *et al*, 1987).

Clauses 7.4 and 7.5 stated that information, claims or comparisons must be capable of substantiation and that such substantiation must be provided in no more than ten days, on request. The Code did not stipulate that substantiation must be within the text of the article. Clause 7.2 required such information, claims or

comparisons to be accurate, balanced, fair, objective and unambiguous. This was indeed the case in this particular instance. Reckitt Benckiser Healthcare therefore considered that there were no breaches of these clauses to answer with regard to this matter.

Alleged breaches of Clause 4

As discussed above, this was not an advertisement. This was an educational article written by the editors of The Practitioner, and so was not required to carry the non-proprietary name adjacent to the most prominent display of the brand name. In fact, as this was not an advertisement, there was no prominent branding used in the article. There was therefore no breach of Clause 4.6 and Reckitt Benckiser Healthcare reiterated that it did not have final editorial control of the article in its final print format.

Reckitt Benckiser Healthcare submitted that if, when it had provided information to the writers and editors of The Practitioner, it had considered this to be a promotional item, it would have considered the PAGB Professional Code rather than the ABPI Code. The PAGB Professional Code required the inclusion of essential information [prescribing information] but had no requirement for a statement as to where this could be found (Clause 4.6.13 of the PAGB Professional Code referred).

Reckitt Benckiser Healthcare also understood that Clause 4.7 of the Code referred to large journal advertisements where the prescribing information often ran overleaf. The article here was not such an advertisement, but an educational discussion of the comfort cycle and the paediatric asthma algorithm. Reckitt Benckiser Healthcare therefore failed to see how Clause 4.7 applied.

Notwithstanding the above, where there were minor technical differences between the PAGB and ABPI Codes, Reckitt Benckiser Healthcare urged the Authority to exercise restraint in its interpretation of the ABPI Code and subsequent rulings. Ruling a breach of one Code when the same practice was permitted under another could raise complexity and difficulties in administration of the self-regulatory framework of both the ABPI and PAGB, and cause confusion throughout the pharmaceutical industry.

Reckitt Benckiser Healthcare submitted that as this was an educational piece rather than promotional material, the requirement for inclusion of information on adverse event reporting mechanisms did not apply. The argument above also applied: the PAGB Professional Code did not require inclusion of adverse event reporting mechanisms, and Reckitt Benckiser Healthcare would thus not necessarily have communicated this point to the journal editors had they considered the article to be promotional. Where such differences existed between the PAGB Professional Code and the ABPI Code, Reckitt Benckiser Healthcare did not believe that the Authority should rule a breach of Clause 4.10 in the circumstances of this case.

Conclusion

Reckitt Benckiser Healthcare contested that this article was within the scope of the ABPI Code. If the article was considered to be promotional (which Reckitt Benckiser Healthcare disputed), it would encourage GPs to recommend Nurofen for Children to parents, for their later purchase, rather than prescription. This would exempt the article from the ABPI Code and would bring it under the auspices of the PAGB Professional Code. Even if the article fell under the ABPI Code it was educational and not promotional.

If the Authority considered that this educational article came within the scope of the ABPI Code, Reckitt Benckiser Healthcare contested the allegation that it was in breach of Clause 7.2 and Clause 10.1.

Reckitt Benckiser Healthcare noted the technical differences between the PAGB Professional Code and the ABPI Code. Had it considered the article to be promotional, Reckitt Benckiser Healthcare would have borne in mind the PAGB Professional Code and not the ABPI Code when communicating with the editors of The Practitioner, as Nurofen for Children was primarily an OTC product. Reckitt Benckiser Healthcare thus contested the alleged technical breaches of Clause 4.

PANEL RULING

The Panel had first to consider whether the 'Quick Guide' article was covered by the Code. Nurofen for Children was a product which, for childhood fever, the subject of the article in question, could be bought OTC or prescribed; sales data showed that most packs of Nurofen for Children were purchased OTC. The supplementary information to Clause 1.1 of the Code stated that the Code did not apply to the promotion of OTC medicines to members of the health professions when the object of that promotion was to encourage their purchase by the public. Where an advertisement was designed to encourage doctors to prescribe the medicine, then it came within the scope of the Code. An item that promoted for both prescribing and recommending purchase would need to comply with both the ABPI Code and the PAGB Professional Code.

The Panel noted that the 'Quick Guide' article referred to the comfort cycle and how important a parent's perception of therapy was in the management of a child's pain. The article stated that 'Prescribing or recommending a treatment of choice will ultimately benefit both [parent] and child'. The Panel acknowledged that although very few packs of Nurofen for Children were prescribed this was not a relevant factor in deciding whether the ABPI Code applied or not. The article referred to prescribing and thus would encourage some doctors to prescribe Nurofen for Children. The Panel considered that the 'Quick Guide' article fell within the scope of the Code.

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 interests. 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 article at issue was developed after Reckitt Benckiser Healthcare had contacted the publishers with a view to introducing GPs to the concepts of the comfort cycle and the paediatric asthma algorithm. Reckitt Benckiser Healthcare provided relevant information and was able to comment on the final article. Reckitt Benckiser Healthcare paid for the article to be included in the journal. The Panel thus considered that the production of the article had not been a strictly arm's length arrangement. The Panel further noted that the article featured, as part of the heading to both pages, a logo which incorporated the red/orange/yellow 'target' associated with the Nurofen brand. In this regard, the Panel considered that the article was promotional in nature. The Panel thus considered that the company's involvement in the development of the article, together with the use of brand logos, meant that Reckitt Benckiser Healthcare was responsible for its content under the Code.

The Panel considered that at first glance the article appeared to be an educational discussion about how best to manage childhood fever. This impression was strengthened by the statement that the insert had been 'Supported with an unrestricted educational grant from Reckitt Benckiser'. The 'Quick Guide' had been provided as an insert in The Practitioner and was intended to be kept for future reference. The only treatments discussed in the article, however, were paracetamol and Nurofen for Children. The Panel noted the way in which the material had been developed; Reckitt Benckiser Healthcare was inextricably linked to the production of the insert. Given the company's involvement the Panel considered that the article was in effect promotional material for Nurofen for Children. The Panel considered that it was disguised promotion; the declaration of sponsorship implied that it was an independently written educational piece which was not so. A breach of Clause 10.1 was ruled.

The Panel noted Pfizer Consumer Healthcare's submission that 'Medicines for Children' jointly published by the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists' Group recommended paracetamol as first line in fever. The title of the article was 'Best practice in childhood fever – the comfort cycle' but the only treatments referred to were Nurofen for Children and paracetamol. It was stated that Nurofen for Children had emerged as a treatment of choice with parents. A diagram of 'The comfort cycle' featured 'Nurofen for Children' in the middle of a cycle of arrows; one arrow was labelled 'Becomes parent's treatment of choice'. The Panel considered that the diagram implied that Nurofen for Children became the treatment of choice for parents. The Panel further considered that as the article was principally about Nurofen for Children, the title 'Best practice in childhood fever – the comfort cycle' implied that Nurofen for Children had been clinically shown to represent best practice which was not so. The Panel considered that the overall message of the article was misleading as alleged. A breach of Clause 7.2 was ruled.

Reckitt Benckiser Healthcare had not provided any information about the Dover Study other than that mentioned in its response. The Panel noted that the diagram depicting 'The comfort cycle' was referenced to the Dover study which compared the single dose efficacy and multiple dose tolerability of paracetamol 15mg/kg and Nurofen for Children 10mg/kg in paediatric fever. According to Pfizer Consumer Healthcare there was no difference in terms of efficacy between the two medicines as measured by reduction in temperature. However the diagram depicted a four stage cycle of 'Reduces anxiety in children', 'Tackles fever', 'Becomes parent's treatment of choice' and 'Reduces anxiety in parent' and so on. 'Nurofen for Children' appeared in the centre of the cycle. The Panel considered that the diagram implied that because it tackled fever, Nurofen for Children became the parent's choice. A description of the study in the text stated that when compared with paracetamol suspension, parents rated Nurofen for Children as more efficacious. According to Pfizer Consumer Healthcare there was, however, no difference between the two medicines with regard to the primary clinical outcome of reduction in temperature/fever. The Panel also noted that the concept of the comfort cycle was a 'working hypothesis'. The Dover study had not measured anxiety in either the parents or the children. The Panel thus considered the article was not a fair reflection of the results of the Dover study and was thus misleading. A breach of Clause 7.2 was ruled.

Eccleston *et al* was cited in support of the statement 'Anxiety is a measure of pain…'. Eccleston *et al* reported on adolescent chronic pain, not childhood fever, the subject of the insert in question. The patients in Eccleston *et al* ranged from 11 to 17 years (mean 14.45 years) and the study examined emotional distress in adolescent chronic pain patients and their parents and the relationship between the two and adolescent coping. The Panel questioned the relevance of the study in the context of a piece about childhood fever which required only short-term treatment. There was no data to show that the relationship between anxiety and pain in adolescents with chronic pain was the same as in infants with acute pain or fever. Nurofen for Children was indicated for children from 3 months to 12 years of age. The Panel considered that citing Eccleston *et al* was misleading as alleged. A breach of Clause 7.2 was ruled.

The Panel noted that the y axis of the bar chart which depicted the percentage of parents who would use either Nurofen for Children or paracetamol again (as

reported in the Dover study) started at 82%. The resultant height of the bars had the effect of making it look as if twice as many parents preferred Nurofen for Children as preferred paracetamol which was not so. The Panel considered that the use of the suppressed zero was misleading. A breach of Clause 7.8 was ruled.

The Panel noted that on the available information the Dover Study had not measured analgesia. Reckitt Benckiser Healthcare submitted that it was widely accepted that ibuprofen was at least as good as paracetamol and that the superiority of ibuprofen was capable of substantiation citing McGaw *et al* in this regard. The Panel noted that the claim 'At least as good as paracetamol' was not referenced as such nor did the Code require it to be referenced. The Code did not require substantiation to be provided in the article itself but the claim must be capable of substantiation. The Panel considered that readers might assume that the Dover study measured pain/analgesia given that the article stated the data was presented at the International Symposium on Paediatric Pain.

McGaw *et al* compared ibuprofen with acetaminophen in the relief of postextraction dental pain in children aged 8 - 16 with the majority of the children in the 14 - 16 age range. The authors commented that postoperative pain associated with dental surgery was associated with pain and oedema and that ibuprofen's superior analgesic efficacy might be due in part to its anti-inflammatory properties which were not shared by acetaminophen. The Panel considered that in the circumstances the reference to 'excellent analgesia (at least as good as paracetamol)' was misleading and a breach of Clause 7.2 was ruled.

The Panel considered that the most prominent display of the brand name was in the highlighted box labelled 'The comfort cycle' in the bottom left hand corner of the front page of the article. The brand name was not accompanied by the non-proprietary name. A breach of Clause 4.6 was ruled.

The Panel noted that the 'Quick Guide' was provided as a bound-in insert in The Practitioner' it was thus a two page advertisement where the prescribing information appeared overleaf. There was, however, no statement as to where the prescribing information could be found. A breach of Clause 4.7 was ruled.

The Panel noted that Clause 4.10 required that all promotional material, other than promotional aids, must include prominent information about adverse event reporting mechanisms. No such information was given in the 'Quick Guide' at issue. A breach of Clause 4.10 was ruled.

Complaint received 19 January 2007

Case Completed 4 April 2007

PRIMARY CARE TRUST HEAD OF PRESCRIBING v ASTRAZENECA

Conduct of representative

The head of prescribing at a primary care trust (PCT) complained that a representative from AstraZeneca had failed to keep an appointment.

The representative had failed to arrive on time for an earlier appointment but had contacted the PCT and the meeting was rebooked. However the representative neither kept the second appointment nor explained his failure to attend. The PCT considered that this disregard wasted staff time and failed to meet high standards. The complaint had originally been taken up with Abbott (Case AUTH/1914/11/06) but it transpired that at the time in question the representative was employed by AstraZeneca.

The Panel considered that the AstraZeneca representative had been foolish to use his own electronic diary instead of that issued by AstraZeneca as he had been unable to back up his appointment information which had been lost due to a battery failure. By the time the representative contacted the PCT he had already missed his appointment. Although the representative's conduct was regrettable and ill-advised the Panel considered that, on balance, there was no breach of the Code.

The head of prescribing at a primary care trust (PCT) complained about the conduct of a representative of AstraZeneca UK Limited.

The matter had originally been taken up with Abbott Laboratories Limited (Case AUTH/1914/11/06) but it had transpired that at the time in question the representative was no longer employed by that company and so no breach of the Code was ruled. The complainant was so informed and he asked for the matter to be pursued with the representative's new employer, AstraZeneca.

COMPLAINT

The complainant explained that earlier in 2006 the representative from Abbott Laboratories had failed to arrive on time for an appointment but had contacted the PCT and the meeting was cancelled and rebooked. However the representative neither kept the second appointment nor explained his failure to attend. The PCT considered that this disregard wasted staff time and failed to meet high standards.

Given the PCT's experiences the first time around, it was somewhat surprised by the representative's failure to attend the second appointment [when unbeknown to the complainant the representative was now working for AstraZeneca] and further surprised that there was no contact to explain what had happened.

The PCT considered this disregard for the appointment system not only wasted staff time but also failed to meet the high standards it had come to expect of representatives' conduct in performing their business duties.

When writing to AstraZeneca, the Authority asked it to respond in relation to Clauses 15.2 and 15.4 of the Code.

RESPONSE

AstraZeneca stated that the representative had joined its salesforce from Abbott where he had a similar role.

In 2006 the representative in question had used his own personal digital assistant (PDA) to store and record customer appointments, as opposed to his company issued device because he found the satellite navigation facility on his own PDA useful. However as a direct result of this, all information regarding his appointments could not be synchronised with his company laptop. It also meant that appointment information was not backed up anywhere.

In October 2006 whilst the representative was on an initial training course (ITC) his PDA ran out of battery power and he lost all his stored details. The representative consequently told his customers that all his appointment details had been lost and he needed to reconfirm appointments or rearrange.

Unfortunately when he contacted the complainant's PCT, he discovered that he had already missed his appointment. When the representative explained he had lost his customer appointment information from his PDA, the person he spoke to seemed very understanding and implied that it was not a problem and an alternative appointment was offered. It was therefore a little surprising to see the letter of complaint.

The ITC the representative attended included a section on the Code and in particular relevant requirements for the salesforce. Within this the importance of maintaining high ethical standards was emphasised as well as taking personal responsibility in respecting a health professional's time when conducting calls. However in light of this complaint AstraZeneca would revise this training to give guidance when circumstances necessitated the cancellation of appointments.

The representative in question was now required to use his AstraZeneca issued PDA so as to avoid this situation occurring in the future.

AstraZeneca considered that in this particular instance the representative had made every effort to contact his customers with whom he might have had appointments, to let them know that he had lost his diary notes. Unfortunately by the time he spoke with the complainant's PCT his appointment had already been missed. Overall AstraZeneca considered the way in which the representative tried to rectify the problem was professional and timely; he had tried to avoid or minimise inconvenience for his customers and demonstrated his respect for health professionals' time. AstraZeneca thus considered that high ethical standards had been maintained. AstraZeneca regretted that this matter had led to a complaint from the PCT. Given the circumstances AstraZeneca did not believe that there had been a breach of Clauses 15.2 and 15.4.

PANEL RULING

The Panel considered that the representative had been foolish to use his own diary management system instead of that issued by AstraZeneca as he had been unable to back up any of his appointment information. By the time the representative contacted the PCT in question he had already missed his appointment. Although the representative's conduct was regrettable and ill-advised the Panel considered that, on balance, there was no breach of either Clause 15.2 or 15.4.

Proceedings commenced 23 January 2007

Case completed 8 March 2007

GENERAL PRACTITIONER v PFIZER and BOEHRINGER INGELHEIM

Spiriva journal advertisement

A general practitioner complained about the claim 'Help them live life, not a COPD [Chronic obstructive pulmonary disease] life' in a journal advertisement for Spiriva (tiotropium) which was co-promoted by Pfizer and Boehringer Ingelheim. The matter was taken up with both companies.

The complainant noted COPD was a chronic, progressive and incurable disease associated with various symptoms which affected patients' quality of life. Spiriva, like other treatments, improved patients' quality of life to a greater or lesser extent, but, the claim at issue went one step too far and suggested that Spiriva cured COPD. The wording '... not a COPD life' suggested that patients would not be troubled by any ongoing symptoms once treatment with Spiriva was initiated. This was misleading and exaggerated the fact that whilst Spiriva would improve clinical outcomes it would never permit patients to live a life free of COPD ie 'not a COPD life'.

In the Panel's view the intended audience would be well aware that COPD was incurable and that treatment was aimed at the alleviation of symptoms. The Panel did not consider that the advertisement would mislead readers into thinking that Spiriva was different in that regard. Further, the claim stated '*Help* [emphasis added] them live life, not a COPD life'. The Panel did not consider that the claim implied that Spiriva cured COPD as alleged. No breach of the Code was ruled.

A general practitioner complained about a journal advertisement (ref SPI/SPV 1445) for Spiriva (tiotropium) which was co-promoted by Pfizer Limited and Boehringer Ingelheim Limited. The matter was taken up with both companies which submitted identical responses.

COMPLAINT

The complainant noted that the advertisement stated 'Help them live life, not a COPD life'. An indisputable fact was that COPD [chronic obstructive pulmonary disease] was a chronic, progressive and incurable disease which was associated with various symptoms which affected patients' quality of life. Also indisputable was the fact that, like Spiriva, there were other treatments which positively impacted patients' quality of life, to a greater or lesser extent. However, the above unqualified claim went one step too far and suggested that Spiriva was a curative treatment for COPD. The wording '... not a COPD life' promoted the position that patients would not be troubled by any ongoing symptoms of COPD once treatment with Spiriva was initiated. This claim was misleading and exaggerated the fact that whilst Spiriva would improve clinical outcomes it would never abolish the effects of COPD completely or otherwise, such as to permit patients to live a life free of COPD ie 'not a COPD life'.

When writing to Pfizer and Boehringer Ingelheim, the Authority asked them to respond in relation to Clauses 7.2, 7.4 and 7.10 of the Code.

RESPONSE

The companies acknowledged that COPD was a chronic progressive and incurable disease which was associated with various symptoms - breathlessness, cough, wheeze - which affected patients' quality of life and referred to the following quotation from a British Lung Foundation (BLF) booklet, 'What is COPD':

> 'COPD can lead to feelings of anxiety because of breathlessness. People with it may reduce their activities to avoid becoming breathless. But by reducing activity levels you become less fit and therefore get breathless even sooner when you try to do any activity. People with COPD may adapt their lifestyles to reduce breathlessness.'

The overall quality of life for people with advanced COPD was about four times worse than for those with severe asthma when the two were assessed using similar quality of life questionnaires (BLF Lung Report III). The problems of restricted mobility were compounded by social isolation and poor self-esteem. A Breathe Easy survey found that 90% of COPD patients were unable to participate in socially important activities such as gardening or going dancing, two-thirds were unable to take a holiday because of their disease and one-third had socially disabling breathlessness (BLF Lung Report III). The claim at issue referred to the quality of life of COPD patients such as that described in this report.

'Help them live life, not a COPD life' referred to Spiriva's ability to improve patient-centred outcomes like breathlessness, exercise tolerance and quality of life. References were clearly cited in the advertisement.

'Help them live life, not a COPD life' referred to Spiriva as part of the management of COPD which ***helped*** patients to achieve a better quality of life. It was not meant as life without COPD, as it was widely accepted (including by the complainant) that COPD was a chronic, progressive and incurable disease.

The companies had not claimed that Spiriva was a curative treatment for COPD or that patients would not be troubled by any ongoing symptoms of COPD once treatment with Spiriva was initiated. But they had claimed that treatment with Spiriva might help patients lead a more normal life.

The companies did not consider that the advertisement was in breach of Clauses 7.2, 7.4 and 7.10 of the Code.

PANEL RULING

In the Panel's view the intended audience would be well aware that COPD was incurable and that treatment was aimed at the alleviation of symptoms. The Panel did not consider that those reading the advertisement would be misled into thinking that Spiriva was different in that regard. Further, the claim stated **'Help** [emphasis added] them live life, not a COPD life'. The Panel did not consider that the claim implied that Spiriva was a curative treatment for COPD as alleged. No breach of Clauses 7.2, 7.4 and 7.10 was ruled.

Complaint received	24 January 2007
Case completed	12 March 2007

CASE AUTH/1956/2/07

GENERAL PRACTITIONER v PFIZER

Exubera journal advertisement

A general practitioner alleged that a full page journal advertisement for Exubera (inhaled insulin human), issued by Pfizer, was misleading because the picture of the inhaler did not give an accurate impression of how large, bulky and inconvenient the device actually was (larger than a pint milk bottle). He had assumed the device would be approximately the same size as a Ventolin inhaler. This would certainly impact on his discussions with patients and his recommendations.

About two thirds of the advertisement was taken up by a photograph of a woman's face and head. In a separate photograph, to one side of the woman's face, the inhaler measured about 7.5cm which, on the photograph of the woman, was about the same distance between her chin and the bridge of her nose.

The Panel considered that readers would assume that the scales of the two photographs were the same which was not so. The inhaler had been shown to a smaller scale than the patient. The Panel considered that on balance the advertisement gave a misleading impression of the size of the inhaler. A breach of the Code was ruled.

A general practitioner complained about a full page journal advertisement (ref EXU658M) for Exubera (inhaled insulin human) issued by Pfizer Limited.

The advertisement had been published in the BMJ 16 December 2006 and 2, 6 and 20 January.

About two thirds of the advertisement was taken up by a photograph of a woman's face and head. Her mouth was highlighted by a white band which was lighter than the rest of the photograph and extended across the page both sides of her face. The band included a claim 'The new look of insulin' on one side and the other side the band drew the reader's eye to a photograph of the Exubera inhaler. The picture of the inhaler in the advertisement measured about 7.5cm which, on the photograph of the woman, was about the same distance between her chin and the bridge of her nose.

COMPLAINT

The complainant alleged that the advertisement was misleading because the picture of the inhaler did not give an accurate impression of how large, bulky and inconvenient the device actually was. This was demonstrated by the administration guide from the company's website.

The complainant had seen the advertisement on several occasions and had assumed that the device would be approximately the same size as a Ventolin inhaler or a Beconase nasal spray. It was only when he saw one demonstrated that the complainant appreciated how bulky it was (larger than a pint milk bottle). This would certainly impact on his discussions with patients and the recommendations he made to them.

The complainant alleged a breach of Clause 7.8.

When writing to Pfizer, the Authority asked it also to respond in relation to Clause 7.2 of the Code.

RESPONSE

Pfizer stated that the Exubera device was represented separately to the woman's face in the advertisement and was not to scale. Generally in advertising, it was unusual for the product being advertised, if represented at all, to be exactly to scale given the constraints of advertising space. The intention of the advertisement was that the inhaler be viewed in terms of how it appeared in isolation as when removed from its packaging in its closed form and not to represent its convenience of use, its technology, nor to compare it relatively. It was simply to give a health professional an idea of what the device looked like. Pfizer decided to include a picture of the device as it believed it appropriate to do so being a new medicine for adult diabetics with a different route and method of administration and to convey an impression of the device. The area around the woman's mouth had been highlighted in white to illustrate that Exubera was inhaled rather than injected.

Details on how to use the Exubera inhaler was in the patient instruction manual on the inhaled insulin (INH) health professional and patient websites (www.inhprogramme.co.uk) as well as in other materials. These illustrations were of an individual patient representing how the device should be used to administer a dose of insulin.

Further, it was clearly illustrated in the advertisement that the device was for holding in the palm of the hand and the fingers to be placed in the indentations on the blue handle as shown and that it would not be small enough to hold between the thumb and finger(s) like an asthma inhaler or nasal spray for example.

The promotional material for Exubera was pre-vetted by the Medicines and Healthcare products Regulatory Agency (MHRA). This included the Exubera advertisement and the inhaled insulin (INH) website.

Pfizer had introduced a dedicated programme of support to health professionals and since the launch of

Exubera in August 2006, representatives had demonstrated the use of the Exubera device to consultant diabetologists, respiratory physicians, GPs with an interest in diabetes, diabetes specialist nurses and pharmacists at each initial call. This had given the health professionals an opportunity to look at and test the device themselves. The illustration of the Exubera device in the advertisement should therefore be considered simply as a reminder to the health professional of the availability of a new inhaled form of insulin and what the inhaler device looked like, but was not intended for making a judgement on its size, weight or how the device should be used.

In summary, Pfizer believed that the advertisement which had been through regulatory review, represented the Exubera inhaler device clearly, accurately and unambiguously and was not misleading as to the nature of Exubera in the context as illustrated. Pfizer therefore denied breaches of Clause 7.2 or 7.8 of the Code.

PANEL RULING

The Panel noted that Exubra was a new product and so in that regard advertisements such as the one at issue might be the first time that many health professionals would have seen the inhaler device. Health professionals would be extremely familiar with inhalers used to treat asthma and so, unless given reason to think otherwise, it was not unreasonable that they might think a device for inhaled insulin would be of a similar size. The Panel noted Pfizer's comments about the use of scale in advertising but considered that in this instance the juxtapositioning and comparative size of the two photographs, one of the patient and the other of the device, were relevant.

The Panel considered that readers would assume that the scales of the two photographs were the same which was not so. The design of the advertisement reinforced this impression by the use of the white band across the advertisement to link the patient's mouth and the inhaler. The inhaler had been shown to a smaller scale than the patient. Contrary to Pfizer's submission the Panel did not consider that the photograph of the inhaler clearly showed that it was not small enough to hold between the thumb and fingers.

The Panel considered that on balance the advertisement gave a misleading impression of the size of the inhaler. The artwork was misleading. Thus the Panel ruled a breach of Clause 7.8. The Panel considered its ruling of a breach of Clause 7.8 covered Clause 7.2.

Complaint received 12 February 2007

Case completed 19 March 2007

CASE AUTH/1957/2/07

ANONYMOUS MEMBER OF THE PUBLIC v SANOFI-AVENTIS

Statements to the public about Lantus

The anonymous mother of a diabetic child alleged that an athlete had promoted Lantus (insulin glargine) to members of the public during a local hospital fun day which she and her son, a type 1 diabetic, had attended. The matter was taken up with Sanofi-Aventis.

The complainant explained that while the children were playing, she was invited, with the other parents, to a presentation on sports and insulin, which interested her a lot, as her son was a keen footballer. One of the speakers gave a very impressive presentation on his sporting successes. The complainant was very interested in how well he managed to control his sugars. He kept referring to an insulin called Lantus and how good it was. The complainant also looked at his website and was very impressed.

The complainant stated that she naturally thought her son would benefit from Lantus, as he sometimes found it difficult to get the balance of sugars right, especially during the start of training for the football season. The complainant spoke to her son's consultant who seemed a bit annoyed (sometimes he was very busy) and stated that it had taken him years to get him stable on his current insulins, and that patients should not be talking about their treatments like this.

The complainant then spoke with her GP who suggested she contact the Authority because she had found out from one of the other parents afterwards that the speaker was sponsored by a pharmaceutical company.

The Panel noted that the speaker was a known Lantus user and that Sanofi-Aventis, *inter alia*, facilitated his appearance at patient group meetings to talk about his personal experience of diabetes and consequently his treatment. As explained by Sanofi-Aventis it would be impossible for him to talk only about his diabetes without mentioning his treatment.

The Panel noted Sanofi-Aventis' submission that the speaker's story inspired those who heard it. The Panel acknowledged that the speaker was expressing his own opinion about his treatment with Lantus but considered that those opinions would have been well known to Sanofi-Aventis which knew that he used Lantus and was very positive about its benefits. The section of the speaker's website which detailed diabetes management referred specifically to Lantus and stated, *inter alia*, 'Lantus allows me more flexibility so I race better, eat better and in general feel better so when I walk up to the start line I know I can race 100% just like everyone else'.

The Panel considered that, given the arrangements that existed between them, Sanofi-Aventis was responsible under the Code for statements made by the speaker at the meeting in question. If it were otherwise then the effect would be for companies' support of patients known to be positive about their products to be used as a means of avoiding the restrictions in the Code.

The Panel noted that it had not been provided with either a copy of the presentation or a transcript of what had been said at the fun day meeting although from the complaint it was clear that the speaker had commented positively about Lantus. The Panel considered that the balance of probability was, that during his talk, statements were made by the speaker which encouraged members of the public to ask their doctor to prescribe Lantus; the complainant had certainly been encouraged to do so. A breach of the Code was ruled. The Panel considered that the overall arrangements were such that Sanofi-Aventis had not upheld high standards and a further breach of the Code was ruled.

The Panel was concerned about the arrangements, noting in particular the effect of the presentation on the complainant and the Panel's ruling in this regard. However, in the absence of a more detailed account of precisely what was said it was not possible to determine whether on the balance of probabilities the presentation was, in effect, an advertisement for Lantus to the general public and thus no breach of the Code was ruled in that regard.

The anonymous mother of a diabetic child alleged that an athlete had promoted Lantus (insulin glargine) to members of the public during a local hospital fun day. The matter was taken up with Sanofi-Aventis.

COMPLAINT

The complainant explained that she had a type 1 diabetic son and had attended a hospital fun day. While the children were playing, the complainant was invited, with the other parents, to attend a presentation on sports and insulin, which interested her a lot, as her son was a keen footballer.

One of the speakers, gave a very impressive presentation on his sporting successes. The complainant was very interested in how well he managed to control his sugars. He kept referring to an insulin called Lantus and how good it was. The

complainant also looked at his website and was very impressed.

The complainant stated that she naturally thought her son would benefit from using Lantus too, as he sometimes found it difficult to get the balance of high and low sugars right, especially during the start of training for the football season, when he had a couple of bad hypos last year.

The complainant brought this up with his consultant who seemed a bit annoyed (sometimes he was very busy) and stated that it had taken him years to get him stable on his current insulins, and that patients shouldn't be talking about their treatments like this.

The complainant then spoke with her GP who suggested she contact the Authority because she had found out from one of the other parents afterwards that the speaker was sponsored by a pharmaceutical company.

When writing to Sanofi-Aventis the Authority asked it to respond in relation to Clauses 2, 9.1, 20.1 and 20.2 of the Code.

RESPONSE

Sanofi-Aventis explained that the speaker first became known to the company in 2005 when he sought support to compete in the world championships. This arose after he came to know a company employee through his athletic club, and as a person with diabetes made a request through them for sponsorship. A sum of £1,000 was freely given to support his world championship involvement.

The speaker's next involvement with the company was in the form of an appearance at a sales conference, where he gave his perspective of living with diabetes. This was in response to a desire to share an inspirational experience of how successful control of a person's diabetes could affect their success in life. He gave both a moving and impactful description of his successes and how he had managed to progress his sporting achievements to a world stage through optimal self-management of his condition. This talk included all aspects of his therapy, including products manufactured by both Sanofi-Aventis and other companies. For this talk he was paid for the time spent away from work and home; travel/accommodation was arranged by Sanofi-Aventis.

This presentation was so inspiring that it was agreed that his experiences would be valuable to share with health professionals to show that diabetes was far from a limiting disease, but could be compatible with a normal life (or that of an elite athlete). Sanofi-Aventis therefore subsequently commissioned him to speak to small meetings restricted to health professionals on his experience of succeeding with diabetes. From the outset he was briefed on the requirement to present on his own experiences as a patient and not to consider that he was there representing Sanofi-Aventis. He produced his own presentation which was focused on his own experience of diabetes and how his self management strategy impacted his performance, without any company involvement. The presentation referred to the various products used to manage his condition, appropriate to the audience. As would be expected, he was compensated financially for his time whenever he spoke at a Sanofi-Aventis sponsored meeting, (details were provided). Travel and any accommodation expenses had always been repaid at cost.

As regards speaking to patient groups, Sanofi-Aventis knew of a handful of occasions when this had been facilitated by the company, in that he had been proposed as a speaker if asked by meeting organisers for a recommendation. Having made such a recommendation, Sanofi-Aventis then had no further input on the title or content of the presentation, nor had it provided any support or materials in preparation of the presentations. These arrangements included the meeting in question. As regards company attendance at these meetings, a Sanofi-Aventis representative only attended if specifically requested to do so by the organiser, but never to promote specific medicines.

Sanofi-Aventis submitted that it had had no involvement in the choice of topics nor the contents of presentations made at any of these meetings, and nor had it provided any content for inclusion in presentations. In view of this, Sanofi-Aventis did not consider that it had made any attempt to promote medicines either directly or indirectly to the public, and that no breach of Clause 20.1 had occurred. Similarly, as he spoke entirely on his own account without any input or influence from Sanofi-Aventis, the company did not consider it was accountable for any content or answers to questions that he gave and that no breach of Clause 20.2 had occurred.

In terms of support for speaking to patient groups, Sanofi-Aventis paid for time and travel in accordance with the policy outlined above. The company considered that it would be unfair not to do so having recommended him as a speaker in the first instance, and the meetings were usually organised with little or no budget available to the organisers and would not go ahead without this support. A payment was made to support his attendance at the meeting in question.

Finally, there was no doubt that the speaker was an inspiration through his achievements within sport whilst successfully managing his diabetes. Although he had been briefed not to promote individual insulins to the public, he discussed his own treatment (Lantus and other non Sanofi-Aventis products) during presentations to patient groups. He considered that to try and gloss over this would be disingenuous as most patients were very knowledgeable about their own treatments. If he omitted this detail, he was invariably asked the question directly and had to answer regardless. The only way to avoid these discussions would be to stop him making any presentation to the public at all. The impact would be to deprive patients and health professionals of the opportunity to see how elite performance could be combined with diabetes.

This story inspired those who heard it, and rather than reducing confidence in the industry, Sanofi-Aventis was proud to have facilitated the sharing of such a story. This activity had helped many patients improve their own self-esteem and had made a positive difference to their lives, and rather than breaching Clauses 9.1 and 2, facilitating such an encounter was an example of something positive that the industry offered to healthcare. It was with some regret, therefore, that the company had suspended any involvement with him pending the outcome of this case, but hoped that a resolution satisfactory to all could be achieved.

Sanofi-Aventis stated that the complaint had served as a prompt to re-brief him on its requirements as a company, and how he could help these by continuing to focus his presentation on his condition rather than its treatment. In addition, all employees had been re-briefed on the company's rigorous requirements regarding the arrangements for promotional meetings. Sanofi-Aventis, considered, however, that these procedures remained consistent with the requirements of the Code and the maintenance of high standards.

PANEL RULING

The Panel noted that the speaker was a known Lantus user and that Sanofi-Aventis, *inter alia*, facilitated his appearance at patient group meetings to talk about his personal experience of diabetes and consequently his treatment. As explained by Sanofi-Aventis it would be impossible for him to talk only about his diabetes without mentioning his treatment.

The Panel noted Sanofi-Aventis' submission that the speaker's story inspired those who heard it. The Panel acknowledged that he was expressing his own opinion about his treatment with Lantus but considered that those opinions would have been well known to Sanofi-Aventis; the company knew that he used Lantus and was very positive about its benefits. The section of his website which detailed diabetes management referred specifically to Lantus and stated, *inter alia*, 'Lantus allows me more flexibility so I race better, eat better and in general feel better so when I walk up to the start line I know I can race 100% just like everyone else'.

The Panel considered that, given the arrangements that existed between them, Sanofi-Aventis was responsible under the Code for statements made by the speaker at the meeting in question. If it were otherwise then the effect would be for companies' support of patients known to be positive about their products to be used as a means of avoiding the restrictions in the Code.

The Panel noted that it had not been provided with either a copy of the presentation or a transcript of what was said at the fun day meeting although from the complaint it was clear that the speaker had commented positively about Lantus. The Panel considered that the balance of probability was that during his talk, statements were made by the speaker which encouraged members of the public to ask their doctor to prescribe Lantus; the complainant had certainly been encouraged to do so. A breach of Clause 20.2 was ruled. The Panel considered that the overall arrangements were such that Sanofi-Aventis had not upheld high standards. A breach of Clause 9.1 was ruled.

The Panel was concerned about the arrangements, noting in particular the effect of the presentation on the complainant and the Panel's ruling in this regard. However, in the absence of a more detailed account of precisely what was said it was not possible to determine whether on the balance of probabilities the presentation was, in effect, an advertisement for Lantus to the general public and thus no breach of Clause 20.1 was ruled.

The Panel did not consider that the circumstances were such as to justify a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such use.

Complaint received 8 February 2007

Case completed 11 April 2007

CASE AUTH/1959/2/07

MEDICINES INFORMATION PHARMACIST v GRÜNENTHAL

Versatis brochure

A medicines information pharmacist complained about a brochure entitled 'Overview and Budget Impact Bulletin: Versatis (5% lidocaine medicated plaster) for localised pain of post-herpetic neuralgia [PHN]' issued by Grünenthal.

The complainant noted that a table, 'Results of the Base Care Analysis (Per Patient)' compared various features of Versatis and gabapentin including the total NHS cost of each. The cost for Versatis was stated as £845, for gabapentin it was £718 with £128 stated as the difference. The complainant alleged that it was misleading to state that gabapentin cost £718 for six months' treatment. There were two forms of gabapentin. If capsules were used for a high dose (800mg three times a day) it would cost only £280 for six months using the price from the Drug Tariff February 2007. The complainant suspected that the price of tablets was used and this was misleadingly expensive.

The Panel noted that the complainant had interpreted 'Total NHS cost' as referring only to the acquisition cost of the medicine whereas Grünenthal submitted that the 'Total NHS cost' for gabapentin referred to the total cost of treatment for six months and included, *inter alia*, the costs of consultations and additional medication. The Panel did not consider that the table at issue was sufficiently clear as to what was meant by the term 'Total NHS cost'. The Panel considered that the impression that 'Total NHS cost' only related to acquisition costs was strengthened by a statement in the text above the table of data which did relate to the acquisition costs of Versatis. The Panel ruled that the data in the table was misleading and thus in breach of the Code.

A medicines information pharmacist complained about a 12 page brochure (ref 064/GRTUK/VERS 12/06-12/08) entitled 'Overview and Budget Impact Bulletin: Versatis (5% lidocaine medicated plaster) for localised pain of post-herpetic neuralgia [PHN]' issued by Grünenthal Ltd. The prescribing information for Versatis, on the back page of the brochure, stated that patients could use up to three plasters for up to 12 hours, followed by at least a 12 hour plaster-free interval.

The brochure was mailed to primary care trust (PCT) and hospital budget holders following the grant of Versatis' marketing authorization. It also formed part of a formulary pack used by representatives.

COMPLAINT

The complainant noted that a table of data, 'Results of the Base Care Analysis (Per Patient)' compared various features of Versatis and gabapentin including the total NHS cost of each. The cost for Versatis was stated as £845, for gabapentin it was £718 with £128 stated as the difference.

The complainant alleged that it was misleading to state that gabapentin cost £718 for six months' treatment. There were two forms of gabapentin. If capsules were used to make a high dose, of say 800mg three times a day, it would cost only £280 for six months using the price from the Drug Tariff February 2007. The complainant suspected that the price of tablets was used and this was misleadingly expensive.

When writing to Grünenthal the Authority asked it to respond in relation to Clause 7.2 of the Code.

RESPONSE

Grünenthal submitted that the complainant had misunderstood the table of data. The complainant referred to the **price** of gabapentin whereas the table referred to the total NHS **cost** of gabapentin treatment.

The £718 total NHS cost of gabapentin treatment included not only the medicine acquisition costs but also the total costs for the whole treatment over six months.

Resource utilisation data were included in the health economic model (Markov model), and covered the following:

1 Costs for gabapentin. The calculation had to differentiate between the first month (titration period according to Prodigy guidelines) and the following five months' maintenance treatment.
2 Costs for additional medicine. For some patients (>40%) gabapentin monotherapy did not provide sufficient pain relief in PHN and so they received additional medication (the same was true and calculated for Versatis). Additional medication was calculated based on information from a Delphi panel and according to Prodigy guidelines.
3 Consultations. From English physicians (Delphi panel) the company received estimates on the number of consultations (physicians, nurses or telephone), necessary for titration of gabapentin and within the maintenance phase.
4 Switch medication. For all patients who discontinued gabapentin treatment the medication was documented, which was applied for the remaining months, until the end of the six month period. Switch medication corresponded to Prodigy

guidelines and included a mixture of the treatment armentarium used in PHN.

5 Referrals. The Delphi panel estimated the number of patients who were referred to specialists after dropping-out, discontinuing gabapentin treatment. Accordingly, costs were defined for the referrals.

Respective costs were calculated for six months' treatment with Versatis which resulted in £845 treatment costs.

In conclusion Grünenthal submitted that it had not produced incorrect or misleading information relating to a competitor product.

PANEL RULING

The Panel noted that the data in question appeared on a page headed 'Versatis: clinical effectiveness and budget impact'. Some of the detail relating to the data was explained above the table in question. The cost of Versatis treatment was based on an average of 1.89 plasters used per day which was the weighted mean from clinical trials. It was stated that it had been assumed that treatment would be for a six month period.

The Panel noted that the complainant had interpreted 'Total NHS cost' as referring only to the acquisition cost of the medicine whereas Grünenthal submitted that the 'Total NHS cost' for gabapentin referred to the total cost of treatment for six months and included the cost of the medicine as well as the cost of consultations with health professionals, switch medication for those that discontinued gabapentin, and additional medication when gabapentin alone did not provide sufficient pain relief.

The Panel did not consider that the table at issue was sufficiently clear as to what was meant by the term 'Total NHS cost'; the text above the table did not give sufficient details in this regard. The Panel considered that the impression that 'Total NHS cost' only related to acquisition costs was strengthened by a statement in the text above the table of data which did relate to the acquisition costs of Versatis. The Panel considered that the data in the table was misleading and thus a breach of Clause 7.2 was ruled.

During its consideration of this case the Panel noted that the calculation for Versatis was based on 1.89 plasters per day at an average cost of £4.55 per day. The Panel noted that plasters could be cut to cover the particular site but queried whether it was appropriate to base the calculation on 1.89 plasters when in effect the patient would need two plasters each day even if only 1.89 daily were used. Page 2 of the brochure stated that the anticipated cost of Versatis was £4.57 per day based on an average use of 1.89 plasters per day. The Panel queried whether the total NHS cost for Versatis was actually as stated ie £845. If one patient used 1.89 plasters at a cost of £4.55 (£4.57) per day for six months the cost of medication would be £828.10 (£831.74) leaving £16.90 (£13.26) over for the cost of consultations or additional medication if necessary. The Panel did not have all the data for Versatis but on the information presented in the booklet queried whether the figures for the total NHS costs of Versatis and gabapentin were calculated on a similar basis. The Panel requested that its concerns be drawn to Grünenthal's attention.

Complaint received 6 February 2007

Case completed 20 March 2007

ANONYMOUS CONSULTANT GYNAECOLOGIST v SERONO

International meetings

An anonymous consultant gynaecologist, writing as a concerned clinician complained about invitations from Serono to attend international meetings.

The complainant alleged that quite a few gynaecologists were routinely invited by Serono to attend international scientific conferences abroad (eg recent meetings of the European Society for Human Reproduction and Embryology (ESHRE)), usually in lavish hotels in nice locations, all expenses paid, while others were never invited, in spite of, in the complainant's case, long standing interest and experience in fertility treatment. The complainant queried whether this non-transparent act of inviting some and ignoring others was in reality a reward and inducement for prescribing Serono's medicines disguised as an educational service?

The Panel considered that it was not necessarily unacceptable to sponsor a delegate to attend a conference in successive years. The arrangements including the selection of delegates and the level of hospitality would have to comply with the Code. The Panel noted that 120 different delegates had been sponsored by Serono to attend ESHRE meetings in 2004, 2005 and 2006; five delegates attended all three. Approximately 1 in 5 delegates who attended the meetings in 2005 and 2006 had also attended the meeting in the previous year. The overall costs incurred (including flights) per delegate were £1,184.81, £1,540.64 and £1,118.66 in 2004, 2005 and 2006 respectively.

The Panel noted the breakdown of costs incurred for five other scientific meetings held from March 2006 to date. The Panel had little information before it about the detailed arrangements. The Panel noted the complainant's comments, but considered that it had no evidence to show that either the level of hospitality or the criteria for selecting delegates was inappropriate in relation to the requirements of the Code. No breach of the Code was ruled.

An anonymous consultant gynaecologist, writing as a concerned clinician complained about invitations from Serono Limited to attend international meetings. The complainant had prescribed Serono's Gonal-F for a few years.

COMPLAINT

The complainant alleged that quite a few gynaecologists were routinely invited by Serono to attend international scientific conferences abroad (eg recent meetings of the European Society for Human Reproduction and Embryology (ESHRE)), usually in lavish hotels in nice locations, all expenses paid, while others were never invited, in spite of, in the complainant's case, long standing interest and experience in fertility treatment. The complainant did not know why some individuals were invited but queried whether this non-transparent act of inviting some and ignoring others was in reality a reward and inducement for prescribing Serono's medicines disguised as an educational service?

When writing to Serono, the Authority asked it to respond in relation to Clauses 2, 18.1 and 19.1 of the 2006 Code and the 2003 Code if the meetings took place before 1 May 2006.

RESPONSE

Serono submitted that as the complainant was anonymous it could not confirm or deny whether (s)he was not invited to a meeting. In any event, since (s)he stated (s)he prescribed Serono's products, his/her attendance or otherwise could not properly give rise to any allegation that the decision to invite him/her or not was in some sense influenced by Serono's desire to offer him/her an inducement. The fact the complainant stated that (s)he prescribed Gonal-F and also had not attended any ESHRE meetings showed that invitations to meetings were not extended to Gonal-F users as an inducement to prescribe Serono's products.

Serono made substantial efforts to ensure compliance with the Code. At the last ESHRE meeting the delegates stayed in the Best Western Kampa, a hotel that, in hindsight, was not of an adequate standard. Points were raised during the certification process that were duly dealt with. Restaurants for subsistence were chosen to provide enough private space, reasonable food and close proximity to the hotel. Flights were organised with a view to minimising costs – all using economy low cost airlines.

In relation to sponsorship provided to health professionals to attend meetings where Serono was not the sponsor (these include ESHRE), the individuals requesting the sponsorship were varied (an anonymised list was provided). Serono's sponsorship of them had no bearing on the level of business from the institution where the individual worked.

The individuals invited were split across the UK and generally comprised those that had not already been invited by other companies. This was because Serono was generally late in inviting delegates. Health professionals requested Serono's support for

attendance at meetings such as ESHRE through a variety of channels; prescribers and non-prescribers of Serono's products were sponsored on a first come first served basis. Furthermore, different people were sponsored for different conferences. Some of Serono's delegates were high users, some did not use any product at all, some used a mixture of different products. It could not be concluded, therefore, that Serono extended invitations or sponsorship to attend scientific meetings as an inducement to prescribe.

Serono's certification process was extensive and backed by comprehensive procedures covering every aspect of the business. As of 1 December 2006, Serono required certification by a lawyer as well as the Code requirement for a medical and non-medical signatory. Serono also had put in place an electronic copy approval system.

Serono concluded that there was no evidence either provided by the complainant, who stated (s)he had never attended the meetings about which (s)he complained, or in Serono's records, to substantiate an allegation of breaches of Clauses 2 and 19.1

In response to a request for further information about a cost discrepancy between two meetings held in Barcelona: the Serono Symposium International Function (SSIF) (Dermatology) meeting at £1,711.54 per person and the SSIF (Neurology) meeting at £1,260 per person, Serono provided a complete breakdown of the costs incurred for each delegate (including Serono employees). The reason for the inconsistency was that flights were booked late for the SSIF Dermatology meeting and hence were more expensive. The average cost per flight for the dermatology meeting was £597.68 compared with £415.75 for the neurology meeting.

These costs had been further updated to reflect actual invoices received since Serono's initial response of 15 March, and as such the cost per person for each meeting was £1,618.91 and £1,437.17 for the dermatology and neurology meetings respectively. The only difference between these costs was the difference in flight charges. The reason for this difference was that flights for the latter were booked far later than would have been preferable and so rates were at a premium compared with those arranged for the neurology meeting.

As far as hotel/subsistence arrangements were concerned Serono provided another spreadsheet detailing venues and costs incurred.

PANEL RULING

The Panel considered that it was not necessarily unacceptable to sponsor a delegate to attend a conference in successive years. The arrangements including the selection of delegates and the level of hospitality would have to comply with the Code. The Panel noted that 120 different delegates had been sponsored by Serono to attend ESHRE meetings in 2004, 2005 and 2006; five delegates attended all three. Approximately 1 in 5 delegates who attended the meetings in 2005 and 2006 had also attended the meeting in the previous year. The overall costs incurred (including flights) per delegate were £1,184.81, £1,540.64 and £1,118.66 in 2004, 2005 and 2006 respectively.

The Panel noted the breakdown of costs incurred for five other scientific meetings held from March 2006 to date. The Panel had little information before it about the detailed arrangements. The Panel noted the complainant's comments, but considered that there was no evidence before it to show that either the level of hospitality or the criteria for selecting delegates was inappropriate in relation to the requirements of the Code. No breach of Clauses 18.1, 19.1 and 2 was ruled.

Complaint received 19 February 2007

Case completed 30 April 2007

COMPLAINANT v GLAXOSMITHKLINE

Diabetes patient review service

A complainant alleged that a GlaxoSmithKline representative downloaded a disc on to the practice system. He then, with the practice nurse's knowledge, chose which patients should attend the clinic GlaxoSmithKline was providing and they were then invited. The complainant believed this was a breach of patient confidentiality. The complainant would be very angry if she knew that a representative had access to her personal information and felt it was important to prevent it happening again.

The Panel noted GlaxoSmithKline's submission that the 'representative' at issue was in fact a Diabetes First Associate (DFA) - a non-promotional role.

The Panel noted that once the software was installed a diabetes report which had no patient identifiable information could be generated. The identifying numbers were held in the practice on a spreadsheet. The DFA did not have access to this spreadsheet. The priority patients search criteria were decided by the practice which also decided who attended for review. GlaxoSmithKline submitted that the DFA did not have access to any patient identifiable information at any stage of the process. The DFA in question had installed and demonstrated the software including how to produce mail merge letters to patients. The administrator produced the letters to patients. GlaxoSmithKline submitted that the DFA never had access to the spreadsheet and when using the practice computer was supervised by the practice nurse.

On the basis of the parties' submissions the Panel did not consider that there was sufficient evidence to show that, on the balance of probabilities, there had been a breach of patient confidentiality as alleged, as the DFA had not had access to identifiable patient data. The Panel ruled no breach of the Code.

A complaint was received about the conduct of a representative from GlaxoSmithKline UK Ltd in relation to a clinic provided by the company at a medical centre.

COMPLAINT

The complainant stated that the representative downloaded a disc on to the practice system. He then, with the practice nurse's knowledge, chose which patients should attend the clinic GlaxoSmithKline was providing and they were then invited. The complainant believed this was a breach of patient confidentiality. This was in September 2006. The complainant would be very angry if she knew that a representative had access to her personal information within her GP practice and felt it was important to prevent it happening again.

When writing to GlaxoSmithKline, the Authority asked it to respond in relation to Clauses 2, 9.1, 18.1 and 18.4 of the Code.

RESPONSE

GlaxoSmithKline stated that the service referred to was the Diabetes Patient Review Service (DPRS). This was a non-promotional service provided by GlaxoSmithKline as a service to medicine through non-promotional representatives known as Diabetes First Associates (DFAs). GlaxoSmithKline confirmed that the person referred to as a representative by the complainant was a DFA and had no promotional elements to his role.

The service included:-

- Software installed on the practice database to run audit reports, identify where the practice could improve data reporting and enable a list of priority patients, where the practice might wish to focus its efforts, to be generated.
- The use of external nurses from an independent, third party company to review patients, if required by the practice.

The practice had complete freedom to choose some or all of these services which were offered free of charge, unconditionally and not linked to the promotion of any medicine.

GlaxoSmithKline was confident that the review service, and its execution in this practice, complied with the Code. This service had been the subject of previous complaints that were found not in breach (Cases AUTH/1806/3/06 and AUTH/1809/3/06).

The objective of the DPRS was to work with health professionals to improve the outcomes of patients with Type 2 diabetes. The service aimed to:

- Improve patient health status.
- Provide the practice with a report that outlined progress against GMS contract requirements.
- Provide the practice with a comprehensive diabetes audit.
- Support the practice in diabetes review.
- Provide benefits to the practice in improving the overall health and management of diabetes patients.

Diabetes Patient Review Service outline

The DPRS was implemented against a standard procedure which began with an introduction to the service from a non-promotional representative, the DFA. The representative's role was to outline the review service to the practice and gain signed consent

to proceed from at least two GPs and the practice manager. Once the DFA had agreement to proceed with the review service, the DFA introduced an agency nurse advisor to the practice. The nurse advisors were employed and managed by the agency and were completely independent of any pharmaceutical organisation. The nurse advisor set up a meeting with the practice to explain the program in full and in particular:

- To agree the search criteria for patients and gain signed agreement to define those patients appropriate for review.
- To discuss the practice protocol for diabetes, which was generated by the practice, and ensure that any recommendations made by the nurse advisor were in line with this protocol, that had been agreed by all members of the practice. Any change in an individual's treatment remained the complete responsibility of the GP.
- To discuss groups of patients that were to be reviewed and gain further authorization.
- To agree with the practice appropriate measures to ensure patient confidentiality.

There were a number of documents that must be reviewed and signed prior to commencing the service. These documents ensured that there were clear search criteria, a written protocol and referral system for patients. Included within these documents was an explanation of the nurse advisor having access to patient information and a clear explanation of the use of any data extracted.

The software used was provided by a third party independent of any pharmaceutical company. GlaxoSmithKline gave details of the way in which the software was installed and data and reports generated. The data seen by the DFA only identified patients by a unique identifying (ID) number – this could be decoded by the practice but not by the DFA.

The software could be used to identify and recall 'priority patients' for review. The criteria for priority review eg smoking status, BMI, blood pressure, cholesterol, glycaemic control were decided by the practice which also decided who attended for review.

The DFA did not have access to any patient identifiable information at any stage of this process. The software system ensured that confidentiality was maintained.

GlaxoSmithKline acknowledged the serious nature of this complaint. It had investigated fully and the DFA involved had been interviewed.

The medical centre agreed to proceed with the review and to hold clinics on two days in August 2006.

The complainant stated that **'…a rep from a pharma company downloaded a disc on a practice system…**'. As previously explained, the practice was given software that enabled it to produce a report of its diabetes patients, which it could use to identify which patients it wanted to review, based on which patients would benefit most from a comprehensive review of all aspects of their diabetes. There was no ability to 'download' any information.

The software was installed and demonstrated by the DFA to the practice nurse. This was usual procedure. A spreadsheet was produced, that was anonymised, each line of the spreadsheet referred to a patient by a unique ID number.

The demonstration consisted of viewing the spreadsheet and performing the following actions:

- Data chasing (highlighting gaps in codes, etc, in the data against patients).
- Practice audit and how the patients identified as a potential priority could be exported to a facility that allowed for mailing of letters to attend clinic. This process was carried out by the practice administrator.
- How to generate a practice report by the sending of data to the third party.

A baseline report in the form of a spreadsheet was generated: this could be used to demonstrate pre- and post-clinic performance. At all stages any data displayed in reports or on the computer screen was anonymised. Patients were listed by unique ID number. The ID numbers could only be matched up to a spreadsheet held in the practice. The DFA never had access to this spreadsheet and was never left unattended beside a practice computer - the only time the DFA was beside the practice computer was to install the software or demonstrate its capability and this was done in full view of the practice nurse who supervised his actions.

'…he then, with the practice nurse's knowledge, chose which patients should attend the clinic…'
The DFA did not choose which patients were invited to the clinic. Criteria were drawn up by the practice based on which patients would benefit most from a comprehensive review of their diabetes, blood pressure and lipids and would fulfil the practice's GMS contract requirements. This predefined criteria, decided by the medical centre practice, could be seen in the Type 2 Diabetes Patient Review Service authorization form.

The software compiled a list of priority patients, based on the predefined criteria. The list was by patient ID number and contained no personal information, so the non-promotional representative would not be able to identify individual patients. This list of priority patients was presented to the practice nurse with unique ID numbers: this information was passed to the administrator by the practice nurse to facilitate letter production and thus recall of patients. Patients were again only identified by unique ID number. Under no circumstances did the non-promotional representative decide on or invite the patients to clinic.

'…I believe this is a breach of patient confidentiality…'
The DFA had no access to data/records that could identify or could be linked to particular patients. The software gave patients unique ID numbers and only the practice had access to information identifying these patients. There was a tick box in the program that

could unmask the unique numbers and display names on the spreadsheet. The DFA showed the tick box on the screen to the practice nurse but did not click it.

GlaxoSmithKline took patient confidentiality very seriously and had clear guidelines for staff working in this area to make sure any patient information was confidential. This was an important part of the DFA training. As set out, the review service offered complied with the Code. GlaxoSmithKline assured the Authority that the DFA did not deviate from the process outlined. This was evidenced by paper work enclosed from this practice. This service was offered in full cooperation and agreement with the practice.

Clauses 18.1 and 18.4 of the Code allowed medical and educational goods and services which enhanced patient care, or benefited the NHS and maintained patient care, to be provided as long as such goods or services did not bear the name of any medicine and did not act as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine. GlaxoSmithKline contended that its review service complied with Clauses 18.1 and 18.4 of the Code as it was clear from the protocols and agreements on which this service was strictly based that the service did enhance patient care in terms of identifying and reviewing appropriate patients, as determined by pre-defined criteria and strict protocols agreed with clinicians prior to the implementation of the service; and this service was not an inducement to prescribe, supply, administer, recommend, buy or sell any medicine. The service agreements set out which treatment recommendations clinicians would endorse according to the patients' current clinical regimen from a complete list of appropriate therapeutic options for patients that included, but was not exclusive to, medicines supplied by GlaxoSmithKline. The service was not linked to promotion of any particular product and was offered to the practice unconditionally. All materials clearly stated that GlaxoSmithKline was the provider of this non promotional service and had been certified as required by Clause 14.3.

Promotional representatives were not involved in the DPRS, in fact they were told when a nurse advisor was undertaking DPRS in a practice, that for a period of 2 days either side, no promotional activity could take place.

GlaxoSmithKline had endeavoured to set up beneficial services to patients and the NHS which took account of all aspects of the Code. The provision of a review service was based on informed consent to the service from the practice and the establishment of a number of detailed agreements as to the appropriate activities and actions undertaken. The DPRS provided a comprehensive review of individuals offering a wide range of non therapeutic and therapeutic options. All patient contact was by appropriately qualified staff and all treatment decisions were made by appropriate health professionals within the practice.

GlaxoSmithKline had taken the utmost caution to ensure patient confidentiality was maintained at all times.

GlaxoSmithKline considered that the highest standards had been maintained and that all activities at this practice and by this representative and review service provided complied with all aspects of the Code. Consequently GlaxoSmithKline considered there was no breach of Clause 2.

As far as GlaxoSmithKline was concerned the practice was satisfied with the services provided except for the performance of one of the nurse advisors. Following the first clinic run by a nurse advisor on 5 September, the practice received several complaints from patients. GlaxoSmithKline was told of these complaints by the practice nurse on 6 September, in particular regarding the quality of the clinic. A second clinic run by a different nurse advisor, on 12 September was satisfactory. Copies of the letter of complaint from the practice nurse and the response from GlaxoSmithKline were provided.

PANEL RULING

The Panel noted GlaxoSmithKline's submission that the 'representative' at issue was in fact a DFA - a non-promotional role.

The Panel noted that once the software was installed a diabetes report could be generated. The report had no patient identifiable information. The unique ID numbers were held in the practice on a spreadsheet. The DFA did not have access to this spreadsheet. The priority patients search criteria were decided by the practice which also decided who attended for review. GlaxoSmithKline submitted that the DFA did not have access to any patient identifiable information at any stage of the process. The DFA in question had installed and demonstrated the software including how to produce mail merge letters to patients. The administrator produced the letters to patients. GlaxoSmithKline submitted that the DFA never had access to the spreadsheet and when using the practice computer was supervised by the practice nurse.

On the basis of the parties' submissions the Panel did not consider that there was sufficient evidence to show that, on the balance of probabilities, there had been a breach of patient confidentiality as alleged as the DFA had not had access to identifiable patient data, the Panel ruled no breach of Clauses 18.1, 18.4 and 9.1. It thus followed there was no breach of Clause 2 .

Complaint received 19 February 2007

Case completed 20 April 2007

GENERAL PRACTITIONER v BOEHRINGER INGELHEIM and LILLY

Cymbalta leavepiece

A general practitioner complained that a Cymbalta (duloxetine) leavepiece issued by Boehringer Ingelheim and Lilly, did not have the non-proprietary name immediately adjacent to the most prominent display of the brand name.

The Panel noted that the non-proprietary name did not appear immediately adjacent to the most prominent display of the brand name and a breach of the Code was ruled as acknowledged by the companies.

A general practitioner complained about a Cymbalta (duloxetine) leavepiece (ref CYM637) issued by Boehringer Ingelheim Limited and Eli Lilly and Company Limited. The leavepiece consisted of a single sheet of paper; the front bore promotional messages for Cymbalta whilst the prescribing information appeared on the reverse.

COMPLAINT

The complainant alleged that the leavepiece did not have the non-proprietary name immediately adjacent to the most prominent display of the brand name.

When writing to the companies the Authority requested that they respond in relation to Clause 4.3 of the Code.

RESPONSE

The companies submitted separate responses. Both companies accepted that the non-proprietary name was not immediately adjacent to the most prominent display of the brand name and apologised for the breach; they would endeavour to ensure it was not repeated.

PANEL RULING

The Panel noted that the brand name Cymbalta appeared in prominent text at the top of the front page of the leavepiece and in logo format at the bottom of that page. Although the intervening text referred to 'Cymbalta (duloxetine)' the non-proprietary name did not appear immediately adjacent to the most prominent display of the brand name and a breach of Clause 4.3 of the Code was ruled.

Complaint received	21 February 2007
Cases completed	Case AUTH/1964/2/07 16 March 2007 Case AUTH/1965/2/07 15 March 2007

CASE AUTH/1966/2/07

GENERAL PRACTITIONER v ALK-ABELLÓ

EpiPen 'Dear Doctor' letter

A general practitioner complained about the strapline 'Curing Allergy' in a 'Dear Doctor' letter for EpiPen (adrenaline (epinephrine) auto-injector) sent by Alk-Abelló. The complainant knew of no method of curing any allergic disease and wondered if there was any evidence to substantiate this dramatic claim. The complainant alleged that the claim was unsubstantiated and could be untruthful.

The Panel noted that the 'Dear Doctor' letter headed 'Expect the unexpected' discussed anaphylactic reactions and promoted the EpiPen twin pack. The strapline 'Curing Allergy' formed part of the company logo and appeared beneath the company name.

EpiPen was for immediate self-administration in the emergency treatment of allergic anaphylactic reactions. The Panel considered that whilst the strapline 'Curing Allergy' was part of the corporate logo it was nonetheless an integral part of the promotional material and thus amounted to a product claim. The Panel noted the company's explanation that its printers had mistakenly inserted the strapline at issue in place of 'United Kingdom'. The claim at issue implied that EpiPen cured allergy and that was not so. The claim was inaccurate and incapable of substantiation as alleged; breaches of the Code were ruled as acknowledged by Alk-Abelló.

A general practitioner complained about a 'Dear Doctor' letter (ref 077E) for EpiPen (adrenaline (epinephrine) auto-injector) sent by Alk-Abelló Ltd.

COMPLAINT

The complainant noted that the company logo at the bottom left hand corner of the letter featured the strapline 'Curing Allergy' and queried the validity of this claim. There was nothing in the letter or the other material enclosed in the mailing to suggest that EpiPen cured anaphylaxis; it simply treated the symptoms.

The complainant knew of no method of curing any allergic disease and wondered if Alk-Abelló had any evidence to substantiate this dramatic claim. The complainant alleged that the claim was unsubstantiated and could be untruthful.

Alk-Abelló was asked to respond in relation to Clauses 7.2 and 7.4 of the Code.

RESPONSE

Alk-Abelló acknowledged that it was not possible for anaphylaxis to be cured by the use of EpiPen and it apologised that the inclusion of this particular strapline was missed by its normally rigorous internal procedures. This was not intentional and this particular strapline reflected the company's raison d'être and vision.

The company submitted that its sign-off processes had been followed; however the printers replaced the strapline 'United Kingdom', which should have been used, with 'Curing Allergy' by mistake. Alk-Abelló accepted that the inclusion of this strapline breached the Code; the letter had already been withdrawn and measures taken to prevent this from happening again.

PANEL RULING

The Panel noted that the 'Dear Doctor' letter headed 'Expect the unexpected' discussed anaphylactic reactions and promoted the EpiPen twin pack. The strapline 'Curing Allergy' formed part of the company logo and appeared beneath the company name in the bottom left hand corner of the letter.

The Panel noted that EpiPen was indicated for immediate self-administration in the emergency treatment of allergic anaphylactic reactions. The Panel considered that whilst the strapline 'Curing Allergy' was part of the corporate logo it was nonetheless an integral part of the promotional material and thus amounted to a product claim. The Panel noted the company's explanation that its printers had mistakenly inserted the strapline at issue in place of 'United Kingdom'. It was, however, an established principle under the Code that companies were responsible for acts and omissions of third parties acting on their behalf. The claim at issue implied that EpiPen cured allergy and that was not so. The claim was inaccurate and incapable of substantiation as alleged; breaches of Clauses 7.2 and 7.4 were ruled as acknowledged by Alk-Abelló.

Complaint received	26 February 2007
Case completed	5 April 2007

PRIMARY CARE TRUST HEAD OF PRESCRIBING AND PHARMACY SERVICES v NOVARTIS

Conduct of representative

The head of prescribing and pharmacy services at a primary care trust (PCT) complained that a representative from Novartis had stated at a surgery that Exforge (amlodipine and valsartan) was endorsed by the PCT which was not so.

The Panel noted that the parties' accounts differed; it was difficult in such cases to know exactly what had transpired. The complaint had arisen from a conversation between a dispensary manager and the representative but had been submitted by a third party.

The Panel noted there appeared to have been a misunderstanding between the representative and the dispensary manager as to which of Novartis' products had been endorsed by the PCT. When discussing such product endorsement with customers it was beholden upon representatives to be very clear. Diovan (valsartan) had been endorsed by a hospital trust as one of the formulary choices and the representative had been told that local PCTs were going to adopt similar guidance. Novartis stated the representative had not discussed PCT endorsement of Exforge only that the representative would be interested to hear the PCT viewpoint on Exforge. According to Novartis the dispensary manager appeared to accept that a misunderstanding had occurred.

It was not possible to determine where the truth lay. On the basis of the parties' submissions the Panel did not consider that there was sufficient evidence to show that on the balance of probabilities the representative had stated that Exforge was endorsed by the PCT as alleged. The Panel ruled no breach of the Code.

The head of prescribing and pharmacy services at a primary care trust (PCT) complained about comments made by a representative from Novartis Pharmaceuticals UK Ltd in relation to Exforge (amlodipine and valsartan).

COMPLAINT

The complainant stated that one of the PCT pharmacists had reported that, whilst working at a surgery, the Novartis representative claimed that Exforge was endorsed by the PCT.

The PCT had never endorsed the product and the complainant considered that the representative had given misleading information in order to instigate prescribing of the product.

When writing to Novartis, the Authority asked it to respond in relation to Clauses 7.2 and 15.2 of the Code.

RESPONSE

Novartis stated that it knew about the complaint and had already interviewed the pharmaceutical advisor, the dispensary manager and the representative. Such complaints from customers were rare and were taken extremely seriously.

The representative's records confirmed that he visited the surgery in 15 February to meet the dispensary manager. The discussion opened with the representative telling the dispensary manager that the Novartis hypertension portfolio had recently been extended and now offered a third therapeutic option with the addition of Exforge. (The three options were Exforge, Co-Diovan (valsartan and hydrochlorthiazide), and Diovan (valsartan)). The representative then discussed the British Hypertension Society (BHS) guidelines and the patient profile for the use of Exforge, the derivation of the product as a fixed dose combination of valsartan and amlodipine, the efficacy data, the BHS view of fixed dose combinations, the complimentary action of the two active ingredients, the cost and dosing. The representative recalled the dispensary manager stating that she would share this information with colleagues in the practice and arrange a follow up visit. She also said that she was expecting a visit from the PCT pharmaceutical advisor and would discuss Exforge with her. The representative stated that he would be interested to hear the PCT's view of Exforge.

The representative then discussed the use of angiotensin II receptor blockers (ARBs) within the practice and mentioned that as a result of the recent ARB review carried out by a local hospital trust there had been an agreement to include Diovan as one of the formulary choices. Key GPs in the area had told the representative that local PCTs were going to adopt the same guidance as the hospital trust. The feedback provided by the representative therefore referred to PCT endorsement of Diovan but not of Exforge as suggested by the complainant.

The interview with the dispensary manager confirmed the structure and content of the discussion with the representative. She recalled the representative stating that Exforge had been endorsed by the local PCT. However during the review of the areas covered by the discussion she observed that a misunderstanding had clearly occurred and that when the representative had referred to Diovan she had assumed he was still

talking about Exforge. In retrospect she observed that it was strange that the representative should have shown an interest in the PCT's view of Exforge at her forthcoming meeting with the pharmaceutical advisor if this had already been established.

During the interview the dispensary manager was generally very complimentary about the representative and the service that Novartis representatives had provided.

In conclusion it appeared that this confusion had arisen because of a misunderstanding and not as a result of any deliberate attempt by the representative to mislead regarding the PCT's endorsement of Exforge, or indeed as a result of any failing in the ethical standards maintained by the representative.

As a result of these events representatives had been instructed to make the transition between products absolutely clear when speaking with health professionals given the close relationship between Exforge and Diovan.

PANEL RULING

The Panel noted that the parties' accounts differed; it was difficult in such cases to know exactly what had transpired. A judgement had to be made on the available evidence. The complaint had arisen from a conversation between a dispensary manager and the representative but had been submitted by a third party.

The Panel noted there appeared to have been a misunderstanding between the representative and the dispensary manager as to which of Novartis' products had been endorsed by the PCT. When discussing such product endorsement with customers it was beholden upon representatives to be very clear about the matter. Diovan had been endorsed by a hospital trust as one of the formulary choices and the representative had been told that local PCTs were going to adopt similar guidance. Novartis stated the representative had not discussed PCT endorsement in relation to Exforge only that the representative would be interested to hear the PCT viewpoint on Exforge. According to Novartis following discussions with it about the complaint, the dispensary manager appeared to accept that a misunderstanding had occurred.

It was not possible to determine where the truth lay. On the basis of the parties' submissions the Panel did not consider that there was sufficient evidence to show that on the balance of probabilities the representative had stated that Exforge was endorsed by the PCT as alleged. The Panel ruled no breach of Clauses 7.2 and 15.2.

Complaint received 23 February 2007

Case completed 20 April 2007

GENERAL PRACTITIONER v PFIZER

Exubera mailing

A general practitioner complained that a letter about Exubera (inhaled insulin human) looked, on first glance, as if it might be an official communication from the National Institute for Health and Clinical Excellence (NICE) from the prominent statement in the top right-hand corner, 'NICE Technology Appraisal Guidance'. It was only on closer examination that it became clear that it was a marketing letter sent by Pfizer. The complainant alleged that this was deceptive, and probably calculated to be so. The complainant further noted that the letter did not give even a summary of the very restrictive conditions under which Exubera was approved for NHS use by NICE.

The Panel noted that the mailing envelope stated on the front 'Promotional Material enclosed' and the Pfizer logo and address was on the back. If the letter had been placed on the complainant's desk, still folded as from the envelope, then all that was visible was information relating to the NICE technology appraisal guidance on inhaled insulin. The Panel queried whether this was what the complainant meant by the appearance of the letter 'on first glance'. Nonetheless the Panel considered the letter in its entirety ie unfolded.

The Panel noted that the mention of NICE was in a different style and colour to that used by NICE. The Panel did not consider that the letter was disguised promotion; readers would not conclude it was an official communication from NICE. The product logo was given at the bottom of the letter. The Panel also noted that the envelope included the statement 'Promotional Material enclosed', and that the accompanying reply paid card clearly referred to Pfizer. The Panel did not consider the letter was disguised nor that the top right-hand corner reference to NICE guidance had been used in a way that was likely to mislead readers. No breach of the Code was ruled.

A general practitioner complained about an Exubera (inhaled insulin human) mailing (ref EXU812a) sent by Pfizer Limited.

The mailing consisted of a letter, a reply paid card and a copy of the Exubera summary of product characteristics (SPC) and was sent to GPs, retail and hospital pharmacists, pharmaceutical advisors, diabetes nurses, diabetologists, and diabetes clinical assistants.

The letter was headed 'NICE [National Institute for Health and Clinical Excellence] technology appraisal guidance 113 - inhaled insulin for the treatment of diabetes (types 1 and 2)'. It mentioned that the NICE guidance was posted on the NICE website and the Pfizer online inhaled insulin programme.

The top right-hand corner of the letter had a blue box containing 'NICE Technology Appraisal Guidance'. The bottom right-hand corner featured the Exubera product logo which included the non-proprietary name. The letter was signed by Exubera marketing on behalf of Pfizer.

COMPLAINT

The complainant stated that on first glance the letter looked as if it might be an official communication from NICE since the prominent notice at the top right-hand corner of the page stated 'NICE Technology Appraisal Guidance'. On closer examination it was a marketing letter sent by Pfizer. The complainant alleged that this was deceptive, and probably calculated to be so.

By convention the top right-hand corner of most letters showed the address and identity of the writer. The letter stated (in very much smaller print) that it was sent by Exubera marketing on behalf of Pfizer but one had to turn the page to find an address.

The letter did not give even a summary of the very restrictive conditions under which Exubera was approved for NHS use by NICE.

The complaint alleged possible breaches of Clause 10, disguised promotion, Clause 9.4, imitating device, copy slogans, general layout etc and Clause 9.5, NICE was not mentioned but perhaps should be listed at the next revision.

RESPONSE

Pfizer stated that the mailing was sent to alert health professionals to the availability of the NICE final appraisal for prescribing Exubera, which had been posted on the NICE website in December 2006. The letter referred to Pfizer's inhaled insulin website to remind health professionals of its existence if they wanted to obtain further information or request materials.

The mailing was obviously promotional and this should have been immediately apparent as the envelope clearly stated 'Promotional Material enclosed' and thus could not have been mistaken for an 'official' one.

Furthermore it was evident from the letter that the promotional material had been produced by Pfizer and signed by a member of the Exubera marketing team on behalf of the company. The NICE appraisal guidance

had been highlighted to emphasise that the reason for writing the letter was to make health professionals aware of the published guidance and to offer them an opportunity to request further information.

Given that the mailing was not made to appear non-promotional and the material was clearly not disguised, Pfizer did not believe that the material was in breach of Clause 10 of the Code.

To reinforce the obviousness of its promotional nature, the letter was presented in the brand livery and this was consistent with the envelope. The blue header on the top right-hand side of the letter 'NICE technology appraisal guidance', did not imitate the NICE logo or branding and the layout of the letter did not copy the general layout of materials produced by NICE. Pfizer therefore submitted that the mailing was not in breach of Clause 9.4 of the Code.

As Clause 9.5 of the Code did not prohibit mention of NICE in promotional materials, there could be no breach of this clause. There were many precedents for the reasonable dissemination of NICE guidelines in promotional materials.

Pfizer considered that the complainant's criticism was mistaken and did not reasonably reflect the views of other health professionals. In summary Pfizer concluded that the Exubera mailing was not in breach of Clauses 10, 9.4 or 9.5 of the Code.

PANEL RULING

The Panel noted that the envelope in which the letter had been posted clearly stated on the front 'Promotional Material enclosed' and the Pfizer logo and address was on the back. It appeared, however, that the complainant had not seen the envelope. The Panel further noted that if the letter had been placed on the complainant's desk, still folded as from the envelope, then all that was visible was information relating to the NICE technology appraisal guidance on inhaled insulin. The Panel queried whether this was what the complainant meant by the appearance of the letter 'on first glance'. Nonetheless the Panel considered the letter in its entirety ie unfolded.

The Panel noted that NICE was not listed as a body that could not be referred to in promotional material. Thus no breach of Clause 9.5 was ruled. Companies had to ensure that references to NICE in promotional material complied with the Code.

The Panel noted that the top right-hand corner mentioned NICE but in a different style and colour to that used by NICE. The Panel did not consider that the letter was disguised promotion; readers would not conclude it was an official communication from NICE. The product logo was given at the bottom of the letter. The Panel also noted that the envelope included the statement 'Promotional Material enclosed', and that the accompanying reply paid card clearly referred to Pfizer. The Panel did not consider the letter was disguised and no breach of Clause 10.1 was ruled.

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. The Panel did not consider that the top right-hand corner reference to NICE guidance had been used in a way that was likely to mislead readers. Thus no breach of Clause 9.4 was ruled.

Complaint received 5 March 2007

Case completed 18 April 2007

GENERAL PRACTITIONER v BAYER

SortEDin10 campaign

The Director of the Authority noted an article in the Financial Times on 17 February critical of the SortEDin10 disease awareness campaign relating to erectile dysfunction (ED) run by Bayer Healthcare. The Director wrote to the author, a general practitioner, drawing attention to relevant cases already considered, pointing out that one element of her criticism had not previously been considered. It was established practice to follow up media criticism of the promotion of prescription medicines. The author subsequently submitted a complaint.

The complainant stated that the criticisms were primarily that the advertisements encouraged men to think that ED could be 'sorted' in 10 minutes. A GP consultation might typically be that long; however this did not reflect the time that would be needed over several consultations for physical examination, exploration of psychological issues and follow up. Prescribing medication was realistically possible in 10 minutes but did not allow time for medical care to encompass the problem fully. In this way the advertisement pushed expectations that something would be 'sorted' in 10 minutes but in fact this would only be the start of the intervention. This was not fair on patients or doctors. It was unrealistic and unhelpful as information as it was so biased.

The Panel noted that the material was aimed at those who believed they had erectile dysfunction but who were too embarrassed to make the initial approach to their GP. Given the embarrassment that might be associated with erectile dysfunction and patients' reticence when discussing it, the Panel considered that the phrase 'SortEDin10' in the advertisements at issue referred to the fact that a ten minute GP consultation would be a significant first step along the road to addressing the condition. In that regard the Panel noted Bayer's submission that, at their first GP visit, a significant proportion of men would be prescribed Cialis, Levitra or Viagra and that these medicines were effective in around 80% of patients. Nonetheless, the Panel did not consider that members of the public would be led to believe that erectile dysfunction would be completely resolved by a GP after one ten minute consultation. No breach of the Code was ruled.

The Director noted an article in the Financial Times on 17 February critical of the SortEDin10 disease awareness campaign relating to erectile dysfunction (ED) run by Bayer Healthcare, Pharmaceutical Division. The Director wrote to the author, a general practitioner, drawing attention to relevant cases already considered, pointing out that one element of her criticism had not previously been considered. It was established practice to follow up media criticism of the promotion of prescription medicines. The author subsequently submitted a complaint.

COMPLAINT

The complainant stated that the criticisms were primarily that the advertisements encouraged men to think that ED could be 'sorted' in 10 minutes. A GP consultation might typically be that long; however this did not reflect the time that would be needed over several consultations for physical examination, exploration of psychological issues, probably also blood tests, and follow up. Prescribing medication was realistically possible in 10 minutes but did not allow time for medical care to encompass the problem fully. In this way the advertisement pushed expectations that something would be 'sorted' in 10 minutes but in fact this would only be the start of the intervention. This was not fair on patients or doctors. It was unrealistic and unhelpful as information as it was so biased.

When writing to Bayer the Authority asked it to respond in relation to Clause 20.2 of the Code.

RESPONSE

Bayer submitted that SortEDin10 was a disease awareness programme designed to support men with ED. The launch in 2005 included national advertisements which ran until September 2005 and aimed to raise awareness of the campaign. Copies of these advertisements were provided. Currently, SortEDin10 took the form of patient leaflets (provided) which were distributed in surgeries and clinics, and a website which was currently being rectified and would be live again in April.

The objective of SortEDin10 was to encourage men who believed they had ED, and were typically too embarrassed, to make that initial approach to their GP. This would be for assessment and where appropriate, treatment.

Ten minutes reflected the average length of a planned GP consultation. The aim of SortEDin10 was to reflect what was normal in general practice and not to mislead or raise unfounded hopes. During a ten minute consultation the patient's ED could be treated in a number of ways with or without medicines. Some of the non-medicinal treatment options, eg change of existing medication for another condition or lifestyle changes, were likely to be suggested by the GP as part of the initial ten minute consultation. In addition a referral to a psychosexual counsellor could be agreed as an appropriate course of action.

70% of those for whom treatment with medicines was

considered an appropriate course of action typically received a prescription on their first GP visit for ED. 99.9% of these patients would receive a prescription for a PDE5-inhibitor which were effective in around 80% of patients. Bayer believed therefore, that for many men, their first consultation was highly productive.

In summary, SortEDin10 was designed to encourage men with ED to seek help from their GP. Bayer reiterated that SortEDin10 accurately reflected what was normal in general practice during an average planned 10 minute consultation and was neither misleading nor attempted to raise unfounded hopes. Bayer denied a breach of the Code.

PANEL RULING

The Panel noted the complainant's concern that the advertisements in the SortEDin10 campaign pushed patient expectations that erectile dysfunction would be sorted in a ten minute GP consultation whereas the consultation would only be the start of the intervention. The Panel noted that each of the three advertisements provided by Bayer featured the prominent 'SortEDin10' logo accompanied by phrases such as: 'See your GP about your erection difficulties, all it takes is ten minutes' and 'Only a ten minute pit stop. I took a ten minute pit stop to see my GP about my erection difficulties…don't be embarrassed to say to your doctor 'I need ten minutes to talk''.

The Panel noted that the material was aimed at those who believed they had erectile dysfunction but who were too embarrassed to make the initial approach to their GP. Given the embarrassment that might be associated with erectile dysfunction and patients' reticence when discussing it, the Panel considered that the phrase 'SortEDin10' in the advertisements at issue referred to the fact that a ten minute GP consultation would be a significant first step along the road to addressing the condition. In that regard the Panel noted Bayer's submission that, at their first GP visit, a significant proportion of men, for whom treatment with medicines was considered appropriate, would be prescribed a PDE5-inhibiter (eg Cialis, Levitra or Viagra) and that these medicines were effective in around 80% of patients. Nonetheless, the Panel did not consider that members of the public would be led to believe that erectile dysfunction would be completely resolved by a GP after one ten minute consultation. No breach of Clause 20.2 was ruled.

Complaint received 9 March 2007

Case completed 27 April 2007

PFIZER v ALLERGAN

Alleged provision of helicopter trips

Pfizer stated that it had been told by two UK ophthalmologists that, whilst in Las Vegas, Allergan UK had invited them and paid all expenses to go on a helicopter trip to the Grand Canyon and that it took three groups on three days. Breaches of the Code were alleged including a breach of Clause 2. The helicopter trip was not strictly limited to the main purpose of the scientific meeting; such excessive hospitality was a good example of an activity that was likely to, *inter alia*, bring discredit upon the industry as evidenced by the surprise expressed by the two ophthalmologists. Pfizer had asked Allergan about the helicopter trip and it had responded by stating that its activities at the meeting complied with the Code. In the light of the information from the ophthalmologists, however, Pfizer considered that the matter should be investigated further.

The Panel noted that the parties' submissions differed. Pfizer alleged that Allergan had paid for two ophthalmologists to go on a helicopter ride to the Grand Canyon, and had taken three groups in all, but had not submitted any evidence in this regard. Allergan had submitted that although its organising agency had been contacted to assist with arranging flights, in all cases the ophthalmologists had paid the company which organised the trip directly. Allergan had further submitted that neither it nor any part of Allergan had paid for helicopter trips or provided discounts for those who contacted its agency for advice on organising a trip.

The Panel considered that, if UK health professionals had gone on a helicopter trip paid for either partly or wholly by any division of Allergan, or an agent working on its behalf, then the provision of such hospitality would not have complied with the Code. However, on the basis of the material before it the Panel considered that there was no evidence to show that such hospitality had been provided. The Panel thus ruled no breach of the Code.

Pfizer Limited complained that Allergan Limited had paid for UK ophthalmologists to go on a helicopter trip whilst at the American Academy of Ophthalmology (AAO) meeting in Las Vegas in November 2006.

COMPLAINT

Pfizer stated that it had been told by two UK ophthalmologists that, whilst in Las Vegas, Allergan UK had invited them and paid all expenses to go on a helicopter trip to the Grand Canyon and that they took three groups on the Saturday, Sunday and Monday. This was in breach of Clause 19.1 of the Code which stated that 'hospitality must be strictly limited to the main purpose of the event'. The supplementary information to Clause 19.1 stated that 'meetings organised for groups of doctors, other health professionals and/or administrative staff which are wholly or mainly of a social or sporting nature are unacceptable'. The helicopter trip described above was not strictly limited to the main purpose of the scientific meeting and was thus in breach of Clause 19.1. Pfizer also alleged that such a flagrant breach of the Code was in breach of Clauses 9.1 and 2. The Code stated that activities or materials associated with promotion must never be such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry. The excessive hospitality described above was a good example of an activity that was likely to be in breach of Clause 2. The surprise expressed by the ophthalmologists who reported this transgression was evidence of discredit being brought upon the industry. Pfizer had asked Allergan about the helicopter trip and it had responded by stating that its activities at the meeting complied with the Code and were not in breach of either Clause 19.1 or Clause 2. In the light of the information from the ophthalmologists, however, Pfizer considered that the matter should be investigated further as the above activities were in breach of Clauses 19.1 and 2.

RESPONSE

Allergan stated that it was surprised to receive this complaint. It had already told Pfizer that it did not pay for any UK ophthalmologists to go on a helicopter trip to the Grand Canyon.

Allergan had received no evidence or further information to support Pfizer's allegations. Any hospitality provided by Allergan at the AAO meeting was provided in line with Clause 19.1 of the Code and was strictly limited to the main purpose of the event and secondary to the purpose of the meeting (ie subsistence only). The level of subsistence offered was appropriate and not out of proportion to the occasion. Allergan submitted that its activities at the AAO meeting complied with the Code and were certainly not in breach of Clauses 19.1, 9.1 or 2.

Allergan provided a copy of the invitation to the AAO meeting, the registration pack and the delegate pack. The AAO was one of the largest and most important ophthalmic meetings in the world and was regarded as an outstanding educational event.

Allergan provided economy class travel to the AAO meeting and hotel accommodation for 4 nights. Given that the meeting was held in a world famous gambling resort, Allergan took great care to find suitable accommodation, venues for meetings and appropriate hospitality for UK doctors. The hotel was selected

because of its cost (£111 per person per night); it could accommodate all of the Allergan-sponsored delegates from Europe and was suitable relative to the other Las Vegas hotels available meeting the above criteria

Allergan paid for registration for the AAO glaucoma sub-speciality day (for those not already members of the academy) but not for registration at the full congress.

Allergan provided full details of its arrangements which included two specific educational events at the AAO meeting for UK ophthalmologists.

Apart from the above meetings and hospitality all delegates at the AAO meeting, including those from the UK, were free to attend the congress meeting and associated events as outlined in the delegate pack.

Allergan knew that many ophthalmologists attending the AAO meeting arranged helicopter flights over the Grand Canyon. Many tour operators had provided such trips. Allergan had details of those who contacted its organising agency to assist with arranging flights. In all cases the ophthalmologists paid directly to the company which organised the trip. Allergan UK (or any part of the Allergan organisation) did not pay for any helicopter trips or provide any discount or benefit for those who contacted its agency for advice on organising a trip.

Allergan strongly denied the allegation that it had paid for helicopter trips or provided any hospitality which could be considered in breach of Clauses 19.1, 9.1 or 2.

PANEL RULING

The Panel noted that the parties' submissions differed. Pfizer had submitted that Allergan had paid for two ophthalmologists to go on a helicopter ride to the Grand Canyon, and had taken three groups in all, but had not submitted any evidence in this regard. Allergan had submitted that although its organising agency had been contacted to assist with arranging flights, in all cases the ophthalmologists had paid the company which organised the trip directly. Allergan had further submitted that neither it nor any part of Allergan had paid for helicopter trips or provided discounts for those who contacted its organising agency for advice on organising a trip.

The Panel considered that, if UK health professionals had gone on a helicopter trip paid for either partly or wholly by any division of Allergan, or an agent working on its behalf, then the provision of such hospitality would not have complied with the Code. However, on the basis of the submissions before it the Panel considered that there was no evidence to show that such hospitality had been provided. The Panel thus ruled no breach of Clauses 2, 9.1 and 19.1.

Complaint received 13 March 2007

Case completed 26 April 2007

ANONYMOUS v TEVA

Qvar journal advertisement

An anonymous complainant drew attention to an advertisement for Qvar, issued by Teva and published in Pulse, alleging that it was unacceptable to show partially clothed people. The complainant considered that the advertisement undermined the serious nature of medicines and was disrespectful of the intended audience.

The Panel noted that the advertisement featured a photograph of a beach scene with a few bikini clad women, but dominating the picture was a young man in swim shorts blowing up a giant lilo. It appeared to the Panel that the picture illustrated what good lung function could mean in a practical sense. The Panel did not consider that the complainant's view regarding the acceptability of the advertisement would be shared by the majority of the audience.

The Panel did not consider that the advertisement failed to recognise the special nature of medicines or the professional standing of the audience to which it was directed. Similarly the Panel considered that the advertisement was not unreasonable in relation to the requirement that high standards must be maintained at all times. No breach of the Code was ruled.

A complainant writing as an 'Anonymous reader of PULSE', complained about an advertisement (ref IV/QV/AD/02/07) for Qvar (beclomethasone diproprionate) placed by Teva UK Limited in that publication.

COMPLAINT

The complainant noted that the Qvar advertisement prominently displayed partially clothed individuals. The complainant was very surprised that it was acceptable for a pharmaceutical company to implement this particular marketing strategy to attract attention. This strategy undermined the serious nature of medicines and disrespected the professional and academic background of the intended audience.

The imagery contrasted remarkably with that used in advertisements for other products in Pulse and perhaps unfairly reflected negatively on the industry as a whole. The complainant believed that it might also offend sections of the intended audience on a number of levels.

When writing to Teva, the Authority asked it to respond in relation to Clauses 9.1 and 9.2 of the Code.

RESPONSE

Teva did not consider that the Qvar advertisement used partially clothed individuals to attract attention. The focus and most prominent part of the image was a person on a beach holiday blowing up a lilo.

The intention of the advertisement was to suggest that asthmatics could lead a normal life and enjoy normal activities at this time of year, such as going to the beach and blowing up a lilo, an activity that was potentially achievable by someone who was free of their normal asthma symptoms. Teva was fully aware of the serious nature of asthma and did not believe this advertisement undermined the serious nature of medicines.

Market research conducted prior to the publication of the advertisement, with a testing panel of twelve GPs and twelve nurses, showed that the beach scene advertisement was the preferred advertisement. Six different advertisement concepts were presented and the health professionals were asked to identify their preference. In depth interviews were then conducted to further understand the reasoning for their decisions. None of the health professionals stated that the advertisement caused offence or undermined the serious nature of medicine.

On review of Pulse Teva did not believe that the Qvar advertisement was in marked contrast to advertisements for other products. The advertisement at issue was also published in numerous other journals, such as GP, Dispensing Doctor, Mims, Independent Nurse, and Guidelines in Practice. Examples were provided of current and past advertisements contained in the same publication of Pulse and in the other journals in which the Qvar advertisement had appeared. Teva did not consider the imagery in the Qvar advertisement to be fundamentally different to the use of partially clothed people in these advertisements.

In summary, Teva did not consider that the advertisement at issue was in breach of Clauses 9.1 or 9.2 of the Code.

PANEL RULING

The Panel noted that the advertisement featured a photograph of a beach scene with a few bikini clad women, but dominating the picture was a young man in swim shorts blowing up a giant lilo. It appeared to the Panel that the picture illustrated what good lung function could mean in a practical

sense. It was unfortunate that the complainant had considered that the advertisement could offend and that it undermined the serious nature of medicines and was disrespectful to the intended audience. This view would not be shared by the majority of the audience.

The Panel did not consider that the advertisement failed to recognise the special nature of medicines or the professional standing of the audience to which it was directed. No breach of Clause 9.2 was ruled.

Similarly the Panel considered that the advertisement was not unreasonable in relation to the requirements of Clause 9.1 which stated that high standards must be maintained at all times. No breach of Clause 9.1 was ruled.

Complaint received **29 March 2007**

Case completed **27 April 2007**

CODE OF PRACTICE REVIEW – MAY 2007

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

1819/4/06	Media/Director v Roche	Newspaper article about Herceptin	No breach Public reprimand by Appeal Board Audit required by Appeal Board Further audit required by Appeal Board in June/July 2007	No appeal Matter referred by Panel to Appeal Board	Page 3
1857/6/06	**Consultant in Public Health Medicine v Roche**	**Activities regarding Herceptin**	**Breach Clause 20.1**	**Appeal by complainant**	**Page 8**
1888/9/06	**Voluntary admission by Bayer**	**Breach of undertaking**	**Breaches Clauses 2, 9.1 and 22** **Audit required by Appeal Board** **Further audit required by Appeal Board in July 2007**	**Appeal by respondent**	**Page 23**
1895/10/06	**Anonymous v AstraZeneca**	**Inappropriate hospitality**	**Breach Clause 19.1**	**No appeal**	**Page 26**
1899/10/06	**Ex-employee/ Medicines and Healthcare products Regulatory Agency v AstraZeneca**	**Representative call rate frequency**	**Breaches Clauses 9.1, 15.4 and 15.9**	**No appeal**	**Page 39**
1910/11/06	**Sanofi Pasteur MSD v GlaxoSmithKline**	**Cervical cancer disease awareness campaign**	**Breaches Clauses 2 and 3.1**	**Appeal by complainant**	**Page 44**
1911/11/06 and 1912/11/06	**Roche and GlaxoSmithKline v Procter & Gamble and Sanofi-Aventis**	**Disparagement of Bonviva**	**Breaches Clauses 7.2 and 8.1**	**No appeal**	**Page 57**
1913/11/06	**Doctor v Astellas Pharma**	**Representative call rates**	**Breaches Clauses 15.4 and 15.9**	**No appeal**	**Page 60**
1914/11/06	Primary Care Trust Head of Prescribing v Abbott Laboratories	Conduct of representative	No breach	No appeal	Page 62
1915/11/06	**AstraZeneca v Novartis**	**Femara leavepiece and press release**	**Four breaches Clause 7.2 Four breaches Clause 7.3 Breach Clause 7.4 Three breaches Clause 7.10 Breach Clause 20.2**	**Appeal by complainant**	**Page 64**
1917/11/06	Primary Care Trust Senior Pharmacist v Pfizer	Promotion of Champix	No breach	No appeal	Page 72

1919/11/06	Primary Care Trust Head of Prescribing and Medicines Management v Pfizer	Promotion of Champix	No breach	No appeal	Page 74
1921/11/06	Retired Hospital Doctor v Schering Health Care	Advertisement to the public about contraception	No breach	No appeal	Page 77
1923/12/06 and 1924/12/06	**General Practice Pharmacist Practitioner v Bristol-Myers Squibb and Sanofi-Aventis**	**Aprovel and CoAprovel mailing**	**Two breaches Clause 7.2 Two breaches Clause 7.4**	**No appeal**	**Page 79**
1926/12/06	**General Practitioner v Lilly**	**Unsolicited provision of samples**	**Breach Clause 17.3**	**No appeal**	**Page 82**
1927/12/06	Doctor v Sanofi Pasteur MSD	Gardasil journal advertisement	No breach	Appeal by respondent	Page 84
1930/12/06	Principal Hospital Pharmacist v Pliva Pharma	Promotion of generic medicines	No breach	No appeal	Page 88
1931/12/06	Practice Manager v Teva	Conduct of representative	No breach	No appeal	Page 90
1933/12/06 and 1934/12/06	Primary Care Trust Prescribing Advisor v Roche and GlaxoSmithKline	Bonviva leavepiece	No breach	Appeal by respondents	Page 93
1935/12/06	Primary Care Trust Assistant Director of Clinical Services v Trinity-Chiesi	Primary Care Report – CFC-free inhalers	No breach	No appeal	Page 97
1936/12/06	**Paragraph 17/Director v Schering Health Care**	**Advertisement to the public and a website**	**Two breaches Clause 20.2**	**No appeal**	**Page 100**
1937/1/07	Primary Care Trust Head of Medicines Management v Wyeth	Enbrel website advertisement	No breach	No appeal	Page 102
1938/1/07	GlaxoSmithKline v Sanofi Pasteur MSD	Gardasil journal advertisement	No breach	No appeal	Page 104
1939/1/07	Community Respiratory Nurse Specialist v GlaxoSmithKline	Promotion of Seretide Accuhaler	No breach	No appeal	Page 107
1940/1/07	**General Practitioner v Bayer**	**Avelox leavepiece**	**Breach Clause 7.2**	**No appeal**	**Page 115**
1942/1/07	**Member of the Public v Janssen-Cilag**	**Disease awareness campaign on schizophrenia**	**Breach Clause 20.2**	**No appeal**	**Page 116**
1943/1/07	**Primary Care Trust Prescribing Head v AstraZeneca**	**Meeting invitation**	**Breach Clause 9.1**	**No appeal**	**Page 122**
1944/1/07	**Drug and Therapeutics Bulletin/Director v Pfizer**	**Promotion of Exubera**	**Five breaches Clause 7.2 Three breaches Clause 7.4**	**No appeal**	**Page 124**
1945/1/07	**Voluntary Admission by Novartis**	**Promotion prior to grant of marketing authorization**	**Breaches Clauses 3.1 and 9.1**	**No appeal**	**Page 129**

1946/1/07	**Pfizer Consumer Healthcare v Reckitt Benckiser Healthcare**	**'Quick Guide' on childhood fever**	**Breaches Clauses 4.6, 4.7 and 4.10 Four breaches Clause 7.2 Breaches Clauses 7.8 and 10.1**	**No appeal**	**Page 131**
1947/1/07	Primary Care Trust Head of Prescribing v AstraZeneca	Conduct of representative	No breach	No appeal	Page142
1948/1/07 and 1949/1/07	General Practitioner v Pfizer and Boehringer Ingelheim	Spiriva journal advertisement	No breach	No appeal	Page 144
1956/2/07	**General Practitioner v Pfizer**	**Exubera journal advertisement**	**Breach Clause 7.8**	**No appeal**	**Page 146**
1957/2/07	**Anonymous Member of the Public v Sanofi-Aventis**	**Statements to the public about Lantus**	**Breaches Clauses 9.1 and 20.2**	**No appeal**	**Page 148**
1959/2/07	**Medicines Information Pharmacist v Grünenthal**	**Versatis brochure**	**Breach Clause 7.2**	**No appeal**	**Page 151**
1961/2/07	Anonymous Consultant Gynaecologist v Serono	International meetings	No breach	No appeal	Page 153
1963/2/07	Complainant v GlaxoSmithKline	Diabetes patient review service	No breach	No appeal	Page 155
1964/2/07 and 1965/2/07	**General Practitioner v Boehringer Ingelheim and Lilly**	**Cymbalta leavepiece**	**Breach Clause 4.3**	**No appeal**	**Page 158**
1966/2/07	**General Practitioner v Alk-Abelló**	**EpiPen 'Dear Doctor' letter**	**Breaches Clauses 7.2 and 7.4**	**No appeal**	**Page 159**
1967/2/07	Primary Care Trust Head of Prescribing and Pharmacy Services v Novartis	Conduct of representative	No breach	No appeal	Page 160
1970/3/07	General Practitioner v Pfizer	Exubera mailing	No breach	No appeal	Page 162
1973/3/07	General Practitioner v Bayer	SortEDin10 campaign	No breach	No appeal	Page 164
1975/3/07	Pfizer v Allergan	Alleged provision of helicopter trips	No breach	No appeal	Page 166
1982/3/07	Anonymous v Teva	Qvar journal advertisement	No breach	No appeal	Page 168

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, about 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
- the provision of information to the public either directly or indirectly, including by means of the Internet
- relationships with patient organisations.

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 7930 9677
facsimile 020 7930 4554)
By email to: complaints@pmcpa.org.uk.