PRESCRIPTION MEDICINES
CODE OF PRACTICE AUTHORITY

CODE OF PRACTICE REVIEW

NUMBER 27 FEBRUARY 2000

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.

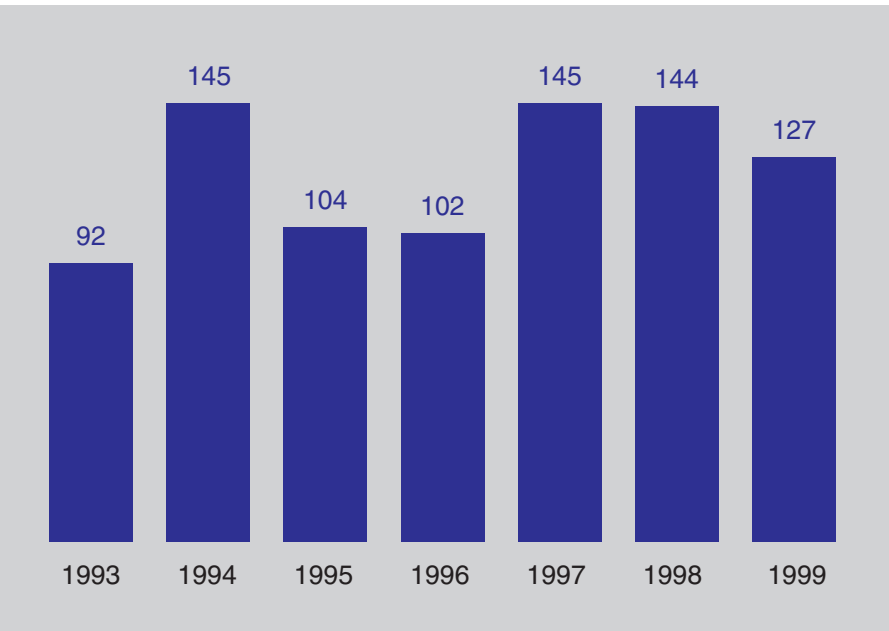
Number of complaints in 1999 down on 1998

There were 127 complaints under the Code of Practice in 1999 as compared with 144 in 1998. There were 145 in 1997 and 102 in 1996.

The number of cases usually differs from the number of complaints because some complaints involve more than one company and because some complaints do not become cases at all, usually because no *prima facie* breach is established. There were 128 cases in 1999 as compared with 138 in 1998.

For only the second time, the number of complaints from other pharmaceutical companies exceeded the number of complaints from health professionals, 48% coming from companies and 38% from health professionals. This was also the pattern in 1996. Usually the greatest number of complaints come from health professionals. The remainder of the complaints in 1999 came from a member of the public, from various organisations and from the Director of the Authority.

Since the Authority was established in 1993, there have been wide but unexplainable variations in the number of complaints received each year, ranging from 92 in 1993 to 145 in both 1994 and 1997.



Making complaints and responding to them

Inter-company complaints are often accompanied by previous correspondence between the parties. While this is helpful, the provision of such correspondence should not be a substitute for clearly setting out the matters complained of in the actual letter of complaint. The Authority cannot be expected to try to tease out from inter-company correspondence the issues which remain unresolved. Similarly, responses which are accompanied by previous correspondence should deal with all of the matters complained of in the actual letter of response.

When multi-issue complaints are made, it is helpful if the issues are numbered in a logical fashion in the letter of complaint and if the same numbering system is used by the respondent.

The co-operation of companies on these points will assist the Authority in the resolution of complaints.

Changes to signatories

Companies are reminded that changes to the signatories who certify promotional material in accordance with Clause 14 of the Code of Practice have to be notified promptly to both the Authority and the Advertising Unit of the Post Licensing Division of the Medicines Control Agency.

Some companies have notified no changes for years and it may be that changes have been made but never notified.

Complying with undertakings

From time to time, claims which have previously been ruled in breach of the Code pop up later in other formats, such as on a forgotten exhibition stand.

Companies are reminded that once they have accepted that a claim etc is in breach of the Code they must ensure that it is removed promptly from all promotional material in whatever form. If representative materials are involved, representatives must be given appropriate instructions in writing to ensure that items in breach do not continue to be used by them and that inappropriate oral statements are not made. Journal advertisements already booked must be cancelled unless it is too late to prevent their further appearance, in which case full details of future appearances must be given on the form of undertaking and assurance.

CODE OF PRACTICE TRAINING

Training seminars on the Code of Practice, open to all comers, are run by the Code of Practice Authority on a regular basis at the Royal Society of Medicine in London.

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

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

Tuesday, 18 April

Monday, 22 May

Friday, 9 June

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 Jean Rollingson for details (020 7930 9677 extn 1443).

How to contact the Authority

Our address is:

Prescription Medicines
Code of Practice Authority
12 Whitehall
London SW1A 2DY

Telephone: 020 7930 9677
Facsimile: 020 7930 4554

Copies of the Code of Practice for the Pharmaceutical Industry and of this Review can be obtained from Lisa Matthews (020 7930 9677 extn 1473).

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.

CASE AUTH/879/5/99

HOSPITAL PHARMACIST v SERVIER

Breach of undertaking

A hospital pharmacist complained about the fourth issue of a journal entitled 'Highlights from … The European Cardiologist – Journal by Fax' sent to him by Servier. He had previously complained about the first issue of this journal which had been ruled in breach of the Code (Case AUTH/721/6/98). Once again his first impression was that the articles appearing in the publication were taken from a well-known journal called 'The European Cardiologist Journal' of which articles contained therein were available by fax on request. This did not appear to be the case. There was a well known periodical called 'The European Journal of Cardiology' which was now called 'The International Journal of Cardiology'. The publication by Servier appeared to be some sort of promotional newsletter. The only difference between it and the one at issue before was that the advertisement for Coversyl no longer appeared on the back page, but on a sleeve that enclosed the publication. The complainant believed that the presentation of articles in this way still did not clearly indicate that the highlights did not come from a published journal, from which papers might be requested, but a collection of faxed articles from cardiologists at the request of Servier. A breach of the Code was alleged in that it appeared to be disguised promotional material.

The Panel noted that the front page was slightly different to that in the previous case. The journal was referred to as 'The European Cardiologist – Journal by Fax' and not as in the previous case 'The European Cardiologist Journal by Fax'. The advertisement for Coversyl now appeared as a wraparound whereas it appeared on the back page of the first edition. The welcome letter on the inside cover was similar in both editions. There were minor differences but in the Panel's view these did not relate to further explanation of the source of the articles. The Panel considered that the journal did not adequately explain the origin of the articles. The letter referred to the articles as being totally independent. The articles had been written by eminent European cardiologists at the invitation of Servier. In the Panel's view it appeared that the articles had been independently generated and presented as a service by Servier. The role of the company in generating the papers had not been made sufficiently clear. The Panel considered that this constituted disguised promotion and a breach of the Code was ruled. With regard to the undertaking given in Case AUTH/721/6/98, the Panel considered that its ruling in the current case of a breach of the Code for similar reasons meant that the company had failed to comply with its undertaking and a further breach of the Code was ruled. The Panel considered that in the circumstances Servier had brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 of the Code was ruled.

Upon appeal by Servier, the Appeal Board noted that there were differences between the material at issue and that considered in Case AUTH/721/6/98; the title of the journal had been changed and there were minor amendments to the welcome letter. The Appeal Board did not consider that these changes were adequate. The material was ruled in breach of the Code for similar reasons to those in Case AUTH/721/6/98 and was thus caught by the undertaking given in that case.

The Appeal Board considered that an undertaking was an important document. The Appeal Board noted that the company had taken steps to comply with the undertaking but the amendments to the material had not been sufficient. The Appeal Board considered that the company's failure to comply with its undertaking brought discredit upon and reduced confidence in the pharmaceutical industry. The Panel's rulings were all upheld.

A hospital pharmacist complained about a mailing sent by Servier Laboratories Ltd. The mailing consisted of a journal entitled 'Highlights from …The European Cardiologist – Journal by Fax'. The Servier logo and company name, together with the statement 'Provided as a service to medicine by Servier Laboratories' were given on the front cover. This was issue number 4 in the series. The inside front cover consisted largely of a 'Dear Colleague' letter from the Assistant Project Manager – Cardiovascular Products. The letter welcomed readers to the fourth edition of the 'Highlights from The European Cardiologist – Journal by Fax' and explained that it was an international postgraduate training service from Servier Laboratories Ltd. The eight annual editions of the mailing would contain a diverse selection of articles from the Journal by Fax all of which were totally independent and written by eminent European cardiologists. Beneath the letter was a list of contributing authors. There then followed five pages of short cardiology papers. The outside back cover carried a corporate advertisement. The journal was enclosed in a wrapper which bore an advertisement for Coversyl.

The first edition of the journal had been the subject of a previous complaint, Case AUTH/721/6/98, from the same complainant.

In addition to Clause 10.1 cited by the complainant the Authority asked Servier to consider the requirements of Clauses 21 and 2 of the Code due to the possibility of a breach of the undertaking given in the previous case.

COMPLAINT

The complainant stated that once again his first impression was that the articles appearing in the publication were taken from a well-known journal called 'The European Cardiologist Journal' of which articles contained therein were available by fax on request.

This did not appear to be the case. There was a well known periodical called 'The European Journal of Cardiology' which was now called 'The International Journal of Cardiology'. The publication by Servier appeared to be some sort of promotional newsletter which it had called 'Highlights from the European Cardiologist – Journal by Fax'. It would seem that

Servier had created some sort of 'fictitious' journal which was not available in any library.

The only difference between this new circular and the one at issue in Case AUTH/721/6/98 was that the advertisement for Coversyl no longer appeared on the back page, but on a sleeve that enclosed the publication.

The complainant believed that the presentation of articles in this way still did not clearly indicate that the highlights did not come from a published journal, from which papers might be requested, but a collection of faxed articles from cardiologists at the request of Servier. A breach of Clause 10.1 of the Code was alleged in that it appeared to be disguised promotional material.

RESPONSE

Servier explained that Servier International was responsible for a service known as 'The European Cardiologist – Journal by Fax'. Eminent European cardiologists were invited to write articles on subjects which they considered of interest to their colleagues. These articles were sent by fax, under the author's name, to cardiologists who had requested to receive them, with a statement that 'The European Cardiologist – Journal by Fax' was supported by an educational grant from Servier.

The subject of this complaint was the fourth edition of 'Highlights from the European Cardiologist – Journal by Fax', which contained five articles selected from 'The European Cardiologist – Journal by Fax'. This piece was produced by Servier Laboratories, and sent as a mailing on 27 April 1999 to senior hospital doctors in cardiology, diabetes, general medicine, geriatrics and clinical pharmacology; GPs with specialist interest in cardiology, hypertension and diabetes; hospital drug information and formulary pharmacists and health authority medical and pharmaceutical advisors.

Although none of the five articles in the fourth edition of 'Highlights from the European Cardiologist – Journal by Fax' mentioned a Servier product, the item was clearly presented as promotional material. It was mailed second class and the envelope had Servier's logo and address on the front and an address label with code number. The format and appearance of the piece was consistent with that of promotional material. The Servier logo and the statement 'Provided as a service to medicine by Servier Laboratories' appeared prominently on the front page. It was sent enclosed in a wrapper on which there was an advertisement for Coversyl 4mg with prescribing information.

Servier did not consider that the 'Highlights' item itself could be considered disguised promotion and denied a breach of Clause 10.1 of the Code.

Servier noted that the complainant's first impression was that the articles were taken from a well-known journal called 'The European Cardiologist Journal' and made available by fax. However, throughout the item, the title was given as 'The European Cardiologist – Journal by Fax' which made it clear that this was a journal which was only available by fax. It was also worth noting that 'The European Cardiologist – Journal by Fax' had been sent to over 7,000 international subscribers 100 times per year for the last 4 years. The International Journal of Cardiology had an international circulation of 500-550 and was sent 15 times per year.

Page 2 of the item consisted of a welcome letter from the Assistant Project Manager – Cardiovascular Products. The letter gave details of 'The European Cardiologist – Journal by Fax' stating that this was an international postgraduate training service from Servier Laboratories Ltd. It described the authorship of the articles and the list of contributing authors was given at the foot of the page. It also explained that the 'Highlights' publication contained a selection of the most interesting articles from 'The European Cardiologist – Journal by Fax'.

In Servier's view, it was made clear to the reader that the 'Highlights' publication came from a Servier produced journal by fax and not from a published journal. The company did not consider that this constituted disguised promotion and denied a breach of Clause 10.1 of the Code.

Servier referred to the Panel's ruling in the previous case (Case AUTH/721/6/98) which was that 'the generation of the papers by Servier was a promotional activity which had been disguised' and that this constituted a breach of Clause 10.1. Servier had sought and been provided with further clarification of the ruling.

Servier reiterated that it took all Code matters very seriously and had discussed how to implement the Panel's previous ruling at length on this case.

In producing the item which was the subject of this complaint, Servier had addressed all the points which the Panel considered ambiguous or unclear. Thus the title was consistently 'The European Cardiologist – Journal by Fax' emphasising that this was a journal only available as a facsimile copy rather than a published journal to be sent by fax.

It has also been made clear on the welcome page that just as the 'Highlights' publication was a Servier service, so too was 'The European Cardiologist – Journal by Fax' a service from Servier International.

The company considered that in accordance with its undertaking and assurance, it had made appropriate changes to the item to avoid further similar breaches of the Code. It therefore denied a breach of Clause 21, and consequently strongly denied a breach of Clause 2.

PANEL RULING

The Panel noted its ruling in the previous case, Case AUTH/721/6/98. The Panel had considered that the title of the mailing 'Highlights From … The European Cardiologist Journal by Fax' gave the impression that it contained extracts from an independently produced journal. In this regard the Panel noted that the letter from the assistant project manager, which welcomed readers to the first edition of the publication, stated that the articles themselves were totally independent. In the Panel's view some readers would assume that the mailing was part of an abstracting, or similar, service. This impression was strengthened by the statement on the front cover 'Provided as a service to medicine by Servier Laboratories'. Although Servier in its response

had consistently referred to 'The European Cardiologist – Journal by Fax', there was no hyphen between the words 'Cardiologist' and 'Journal' on the front cover of the mailing and this made the meaning of the title somewhat ambiguous. The Panel noted that the papers published in the mailing were written at the invitation of Servier International. The authors came from an international group of 41 contributors listed on the inside front cover. The Panel did not consider that the mailing adequately explained the origin of the papers. In the Panel's view, readers of the material might regard the papers differently if they knew how they had been generated. The Panel noted Servier's view that the mailing had clearly been presented as promotional material. The Panel did not consider, however, that the role of the company in the generation of the papers had been made sufficiently clear. It appeared as if Servier was offering an abstracting service from a recognised clinical journal which was not so. In the Panel's view, this constituted disguised promotion and a breach of Clause 10.1 was ruled.

The Panel turned to the case now before it. The Panel noted that the front page was slightly different to that in the previous case. The journal was referred to as 'The European Cardiologist – Journal by Fax' and not as in the previous case 'The European Cardiologist Journal by Fax'.

The fourth edition of the journal was presented differently to the first edition in that the advertisement for Coversyl appeared as a wraparound to the fourth edition whereas it appeared on the back page of the first edition. The welcome letter on the inside cover was similar in both editions. There were minor differences but in the Panel's view these did not relate to further explanation of the source of the articles. The Panel considered that the fourth edition of the journal did not adequately explain the origin of the articles. The letter referred to the articles as being totally independent. The articles had been written by eminent European cardiologists at the invitation of Servier. In the Panel's view it appeared that the articles had been independently generated and presented as a service by Servier. The role of the company in generating the papers had not been made sufficiently clear. The Panel considered that this constituted disguised promotion and a breach of Clause 10.1 of the Code was ruled.

With regard to the undertaking given in Case AUTH/721/6/98 the Panel considered that its ruling in the current case of a breach of Clause 10.1 of the Code for similar reasons meant that the company had failed to comply with its undertaking. There were minor differences in the welcome letter but the Panel considered these to be insufficient as they did not provide further information about the origin of the articles. A breach of Clause 21 of the Code was ruled.

The Panel noted that Clause 2 of the Code was used as a sign of particular censure. Previous cases involving breaches of Clause 21 had also been ruled to be in breach of Clause 2 when material was reused without being altered. The Panel noted that there had been some minor alterations to the material but considered that these were not adequate. The Panel noted Servier's submission regarding the title of the publication and the placement of a hyphen but considered that a 'Journal by Fax' would not be a familiar concept to most readers and so the true nature of the journal would remain unclear. In the Panel's view the first issue and the fourth issue were no different in relation to the explanation about the source of the articles. The Panel considered that in the circumstances Servier had brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 of the Code was ruled.

APPEAL BY SERVIER

Servier stated that Servier International was responsible for a service known as 'The European Cardiologist – Journal by Fax'. Eminent European cardiologists were invited to write articles on subjects which they considered of interest to their colleagues. These articles were sent by fax, under the author's name, to cardiologists who had requested them, with a statement that 'The European Cardiologist – Journal by Fax' was supported by an educational grant from Servier.

The item which was the subject of this complaint was the fourth edition of 'Highlights from the European Cardiologist – Journal by Fax', which contained five articles selected from 'The European Cardiologist – Journal by Fax'. None of the five articles mentioned a Servier product. This piece was produced by Servier Laboratories, and sent as a mailing on 27 April 1999 to senior hospital doctors in cardiology, diabetes, general medicine, geriatrics and clinical pharmacology; GPs with specialist interest in cardiology, hypertension and diabetes; hospital drug information and formulary pharmacists and health authority medical and pharmaceutical advisors.

Servier stated that although none of the five articles in the fourth edition of 'Highlights from the European Cardiologist – Journal by Fax' was promotional in content, the item was in its view clearly presented as promotional material. It was mailed second class and the envelope had Servier's logo and address on the front and an address label with code number. The format and appearance of the piece was consistent with that of promotional material. The Servier logo and the statement 'Provided as a service to medicine by Servier Laboratories' appeared prominently on the front page. It was sent enclosed in a wrapper on which there was an advertisement for Coversyl 4mg.

Servier did not consider that the 'Highlights' item itself could be considered disguised promotion. On the contrary, the first impression was clearly that this was promotional material. Servier noted that the ruling of a breach of Clause 10.1 was in relation to the generation of the articles.

Servier noted that the complainant's first impression was that the articles were taken from a well-known journal called 'The European Cardiologist Journal' and made available by fax. However, throughout the item, the title was given as 'The European Cardiologist – Journal by Fax' which in Servier's view made it clear that this was a journal which was only available by fax. Servier was not aware of any independently produced journal by fax which could be confused with the Servier produced 'The European Cardiologist – Journal by Fax'.

Servier noted the Panel's view that the role of the company in generating papers had not been made sufficiently clear.

Page 2 of the item consisted of a welcome letter from the 'Assistant Project Manager – Cardiovascular Products'. The letter gave details of 'The European Cardiologist – Journal by Fax' stating that this was an international postgraduate training service from Servier Laboratories Ltd. It described the authorship of the articles and the list of contributing authors was given at the foot of the page. It also explained that the 'Highlights' publication contained a selection of the most interesting articles from 'The European Cardiologist – Journal by Fax'.

In Servier's view, it was made clear to the reader that the 'Highlights' publication came from a company produced journal by fax and not from a published journal. Servier therefore did not consider that this constituted disguised promotion and denied a breach of Clause 10.1 of the Code.

Servier noted that the Panel had ruled a breach of Clause 21 as its ruling in this case was similar to its ruling in a previous case, Case AUTH/721/6/98. That case was brought by the same complainant about the first edition of 'The European Cardiologist – Journal by Fax'. The Panel had ruled a breach of Clause 10.1 as the role of the company in the generation of the papers had not been made sufficiently clear.

Servier took all Code matters very seriously and stated that it had sought further clarification of the Panel's ruling, which was given in a letter from the Authority dated 24 July 1998. In producing the item which was the subject of this complaint, Servier had addressed all the points which the Panel considered ambiguous or unclear. Thus the title was consistently 'The European Cardiologist – Journal by Fax' emphasising that this was a journal only available as a facsimile copy rather than a published journal to be sent by fax. It had also been made clear in the welcome page that just as the 'Highlights' publication was a Servier service, so too was 'The European Cardiologist – Journal by Fax' a service from Servier International.

Servier considered that in accordance with its undertaking and assurance, it had made appropriate changes to the item to avoid further similar breaches of the Code and therefore denied a breach of Clause 21.

Servier devoted considerable effort to ensure that promotional material complied with the Code. Servier had considered fully the Panel's ruling in the previous case when producing the item which was the subject of this complaint and therefore strongly denied a breach of Clause 2.

APPEAL BOARD RULING

The Appeal Board noted that there were two related publications 'The European Cardiologist – Journal by Fax' was a compilation of articles produced by a panel of cardiologists and distributed by facsimile by Servier International. Authors wrote short articles on topics which they chose themselves. Occasionally, if a paper had been recently published, Servier International might ask the author to write a short article based on the paper. Authors had editorial control over each article although Servier International chose which articles would be faxed. There were approximately 80 editions of the journal by fax each year, each typically consisting of one or two articles, and they were sent to 3000 cardiologists who had requested the service. About 200 cardiologists in the UK received the service. Servier UK selected articles from the journal by fax to compile the 'Highlights from The European Cardiologist – Journal by Fax'. The 'Highlights' publication was mailed, unsolicited, to 20,000 doctors and pharmacists 8 times a year.

The statement 'Provided as a service to medicine by Servier Laboratories' appeared both on the front page of the 'Highlights' publication and on the envelope in which it was sent. In the Appeal Board's view such a statement was inconsistent with a promotional activity. The Appeal Board considered that the reference to a journal would lead some readers, particularly those with a limited knowledge of specialist cardiology journals, to assume that the publication consisted of abstracts from a journal which existed in its own right in the traditional sense of the word. This was not so.

The welcome letter described 'The European Cardiologist – Journal by Fax' as an international postgraduate training service from Servier Laboratories and stated that the 'Highlights' publication contained a diverse selection of the most interesting articles from 'The European Cardiologist – Journal by Fax'. The articles were described as totally independent. The Appeal Board did not consider that the reader had been provided with sufficient explanation of Servier's role in the generation of the articles and upheld the Panel's ruling of a breach of Clause 10.1 of the Code. The appeal on this point was thus unsuccessful.

The Appeal Board noted that there were differences between the material at issue and that considered in Case AUTH/721/6/98; the title of the journal had been changed and there were minor amendments to the welcome letter. The Appeal Board did not consider that these changes were adequate. The material was ruled in breach of the Code for similar reasons to those in Case AUTH/721/6/98 and was thus caught by the undertaking given in that case. The Appeal Board upheld the Panel's ruling of a breach of Clause 21. The appeal on this point was thus unsuccessful.

The Appeal Board considered that an undertaking was an important document. The Appeal Board noted that the company had taken steps to comply with the undertaking but the amendments to the material had not been sufficient. The Appeal Board considered that the company's failure to comply with its undertaking bought discredit upon and reduced confidence in the pharmaceutical industry and upheld the Panel's ruling of a breach of Clause 2. The appeal on this point was thus unsuccessful.

Complaint received **21 May 1999**

Case completed **17 November 1999**

MEDICINES CONTROL AGENCY v SEARLE and PFIZER

Advance information on celecoxib

The Medicines Control Agency complained about advance information for celecoxib, alleging that it was in breach of the Code because it did not state clearly that celecoxib was not yet licensed and was vague about expected costs and budgetary implications and, furthermore, it appeared more likely to be of interest to prescribers than to those responsible for policy decisions on budgets. The information had been made available by both Searle and Pfizer.

The Panel noted the intended audience, directors of public health and pharmaceutical and medical advisers. The Panel was concerned that the material had been sent to prescribing advisers to primary care groups given that the relevant supplementary information referred to health authorities and trust hospitals etc. The Panel accepted that the supplementary information had been agreed prior to the introduction of primary care groups.

The Panel noted that the exemption for advance information related to the introduction of new medicines or changes to existing medicines which might significantly affect health authorities' and trust hospitals' levels of expenditure during future years. The Panel did not know whether the introduction of celecoxib would significantly affect expenditure in future years because the material did not make this clear. In this regard the Panel noted that the materials did not give sufficient information to enable the reader to determine whether the use of celecoxib to treat arthritis would require more money overall or less money overall. In the Panel's view the companies had not demonstrated that the introduction of celecoxib might significantly affect levels of expenditure in future years. The materials did not explore this in any detail. In the Panel's view therefore the materials should not have been issued at all. A breach of the Code was ruled.

Upon appeal by Searle and Pfizer, the Appeal Board considered that it was appropriate to provide advance information to medical and pharmaceutical advisers and to prescribing advisers in primary care groups. The supplementary information should be updated to make this clear.

The Appeal Board appreciated the need of the NHS to receive information about products prior to them reaching the market. However, the promotion of unlicensed products or unlicensed indications would be in breach of the Code. The exemption in the supplementary information was limited to products which might significantly affect levels of expenditure. The supplementary information stated that the likely cost and the budgetary implications must be indicated and must be such that they would make significant differences to the likely expenditure of health authorities, trust hospitals and the like.

The Appeal Board accepted the difficulties of establishing the price of a medicine before it was launched. The Appeal Board considered that Searle and Pfizer had not demonstrated that the introduction of celecoxib might significantly affect levels of expenditure in future years. The materials did not explore this in sufficient detail. The Appeal Board therefore upheld the Panel's ruling of a breach of the Code.

COMPLAINT

The Medicines Control Agency (MCA) had received a complaint concerning advance material issued by Searle in respect of celecoxib. It had been alleged that the material was in breach of Regulation 3(1) of The Medicines (Advertising) Regulations 1994 [SI 1994/1932, as amended].

The MCA had reviewed the material and did not consider that there had been a breach of Regulation 3(1). However, it considered that the material supplied to health authorities and trust budget holders was in breach of Clause 3.1 of the Code as it did not state clearly that celecoxib was not yet licensed and was vague about expected costs and budgetary implications. Furthermore, it appeared more likely to be of interest to prescribers than to those responsible for policy decisions on budgets. Accordingly, the MCA requested that the matter be treated as a complaint under the Code.

The complaint was taken up with both Searle and Pfizer Limited as the product was being developed by both companies.

RESPONSE FROM SEARLE

Searle did not accept that the material was in breach of Clause 3.1 of the Code, which was essentially the same as Regulation 3(1) of The Medicines (Advertising) Regulations which the MCA believed had not been contravened. Both provisions were aimed at the same harm, namely promotion of an unlicensed medicine. Although the Code provided further information and guidance on the application of Clause 3.1, Searle did not believe it was possible to be in breach of the clause and not the parallel regulation.

Searle believed that it had followed all the guidance in the supplementary information to the Code. The materials referred to by the MCA were two Searle Medical Information fact sheets on celecoxib and COX-2 specific inhibitors and the Searle/Pfizer advance information on celecoxib for health authority and trust budget holders which consisted of four booklets: The Ageing Population, The Burden of Arthritis, COX-1 and COX-2 and Celecoxib Clinical Budgetary Information.

Medical Information Celecoxib Fact Sheet

Searle did not believe that the MCA intended to make the medical information material the subject of complaint as the letter to the Authority referred to 'the material supplied to health authorities and trust budget holders'. However, as outlined below, the medical information fact sheets were not promotional and had been used exclusively to respond to individual requests for information.

As was Searle's practice with all requests for information, each enquirer received a response from the company's medical information department tailored to their questions. There had been considerable interest amongst health care professionals and academics in the relatively new and evolving science of COX-2 inhibition. Much of the interest had been stimulated by the publication of scientific data, and also the introduction of celecoxib in the United States. Over the last 18 months Searle had received a large number of enquiries about COX-2 inhibition in general, and celecoxib in particular. Whilst some enquiries had been about very specific areas of interest, many of them had been requests for either general information about COX-2 inhibition or information on the clinical profile of celecoxib.

In order to help satisfy these requests, two basic fact sheets were prepared at the beginning of 1999: the celecoxib fact sheet, and the COX-2 specific inhibitors fact sheet. Either fact sheet might be used in its entirety to help answer an enquiry, or adapted as required. The fact sheets were always accompanied by a tailored letter from the medical information department.

Searle had records of all the requests for information it received. The majority were from hospital doctors and, of those, over half requested general information on COX-2 with the remainder requesting information on celecoxib. A large minority of requests had also come from hospital pharmacists, with a lesser number from general practitioners, health authorities etc.

In summary, Searle believed that the material and its use was not promotional and did not contravene the Code.

Advance Product Information

Searle stated that as part of the MCA's investigation into the complaint on the fact sheet it requested copies of any material Searle had issued in respect of celecoxib. To this end, copies of the advance information for health authority and trust budget holders were provided.

The complaint from the MCA alleged that the advance product information was in breach of Clause 3.1 as it did not state clearly that celecoxib was not yet licensed and was very vague about expected costs and budgetary implications, furthermore it appeared more likely to be of interest to prescribers rather than those responsible for policy decisions.

Searle did not agree that the material was in breach of the Code. According to the supplementary information to Clause 3.1, companies were permitted to provide information on products which contained a new active substance to those responsible for making policy decisions on budgets. Copies of the advance product information were provided to Searle's NHS liaison team to be used with budget holders (directors of public health, pharmaceutical and medical advisers) to discuss the budgetary implications of the proposed introduction of celecoxib, after determining their wish to receive information. A copy of the advance product information could be left with budget holders following discussions. If a budget holder requested information only, this was provided by the medical information department. Copies of the written instructions to Searle's NHS liaison personnel and the pro-forma letter used by them for budget holders were provided.

The MCA alleged that the advance product information was in breach of Clause 3.1 because it did not state clearly that celecoxib was not yet licensed. It was not a requirement of Clause 3.1 (nor any of the supplementary information accompanying it) to state this. The introductory sentence of the material (Celecoxib Clinical and Budgetary Information) was 'Celecoxib belongs to a new class of agents known as COX-2 specific inhibitors (CSI) of which there are none currently available on the market …….' The second paragraph began 'As a COX-2 specific inhibitor, it is proposed that celecoxib will be indicated for the symptomatic treatment …..' The advance product information had not been 'cold mailed' to budget holders and the letter used by the NHS liaison team further stated 'The product has completed Phase III trials and is being evaluated by Regulatory Authorities …' From this it was clear that no recipient of the information could have been left with the impression that the product was licensed. Searle did not accept that the information was in breach of Clause 3.1 in this regard.

The second issue raised by the MCA was that the advance product information was very vague about expected costs and budgetary implications. Searle did not agree that the information provided was vague. On one page of the Celecoxib Clinical and Budgetary Information a chart was presented showing the range of costs of frequently co-administered therapeutic agents. The potential range of costs for celecoxib was also clearly shown on the chart. The exact price that would be charged for celecoxib was, of course, not finalised at this stage.

The potential budgetary implications of the introduction of celecoxib were outlined on the opposite page of the booklet with a chart showing the areas where the use of celecoxib would increase costs (eg if used in place of generic NSAIDs) and where its use might be expected to reduce costs (eg by reducing the costs of secondary care associated with serious gastrointestinal events). The chart did not set out to describe the exact impact of celecoxib as this would be affected by decisions made on the population the product was used in, the product(s) it was used in place of etc. However, it did identify the areas of expenditure where the use of celecoxib could make significant differences to a health authority. Searle believed that the information on the costs of current medicines, the likely costs of celecoxib, and the potential budgetary implications, whilst not prescriptive, was not vague and provided appropriate advance information to budget holders to plan and estimate their future budgets.

In conclusion Searle believed that the advance product information material it had produced and the way in which it had been used was in accordance with Clause 3.1 of the Code.

RESPONSE FROM PFIZER

Pfizer stated that the response from Searle should be treated as the response from Pfizer. However, for the sake of clarity and completeness Pfizer provided

details of exactly how the material complained of was used by Pfizer.

Searle Medical Information Material

Pfizer's medical information department started taking enquiries on celecoxib from 1 June 1999. Since then there had been 28 enquiries, the majority of which had been answered verbally without the need to send out information. In six cases the standard Searle celecoxib medical information had been sent to enquirers who had been health authority pharmaceutical/medical advisers, one GP, one hospital pharmacist and one hospital doctor. Pfizer would always send the information under a covering letter.

Advance Product Information

The advance product information consisted of the four booklets referred to by Searle, which were prepared with the aim of raising the awareness of NHS budget holders to the importance of appropriate management of pain and arthritis and to demonstrate the new benefits which the COX-2 technology and celecoxib would bring. The advance product information was distributed to Pfizer's customer healthcare consultants (CHCs) who were NHS liaison personnel. The CHCs worked with NHS management at various levels on a wide variety of health issues and principally dealt with non-prescribers and others involved in NHS management in a non-prescribing capacity.

The advance product information was issued to Pfizer CHCs in January 1999, accompanied by a briefing note. This briefing note was not used by Searle. Pfizer also issued a one page guidance note. Pfizer did not issue to the CHCs the pro forma covering letter sent to Searle NHS liaison personnel.

Pfizer's CHCs used the advance product information in the same way as Searle's NHS liaison team, ie only with NHS personnel having budgetary policy responsibilities, such as directors of public health, medical and pharmaceutical advisers to health authorities etc and prescribing advisers to primary care groups.

For the reasons explained by Searle, Pfizer did not believe that any of the material referred to was in breach of Clause 3.1 of the Code either inherently or in the way in which it had been used.

PANEL RULING

The Panel noted that Clause 3.1 of the Code stated that a medicine must not be promoted prior to the grant of the marketing authorization which permitted its sale or supply. The supplementary information to Clause 3.1 stated that health authorities and trust hospitals needed to receive advance information about the introduction of new medicines which might significantly affect their level of expenditure during future years. At the time such information was required the medicines concerned would not be the subject of marketing authorizations and promotion of them would thus be in breach of the Code. Information on such medicines could, however, be provided as long as the information related to a new active substance, an active substance prepared in a new way, a significant new indication for an existing product or a product with a novel and innovative means of administration. Such information should be directed to those responsible for making policy decisions on budgets rather than those expected to prescribe. The likely cost and budgetary implications must be indicated and must be such that they would make significant differences to the likely expenditure of health authorities and trust hospitals and the like. Only factual information must be provided which should be limited to that sufficient to provide an adequate but succinct account of the product's properties. The information should not be in the style of promotional material and should not include mock up drafts of summaries of product characteristics. If requested further information could be supplied.

The Panel noted that the MCA considered that the material supplied to health authorities and trust budget holders was in breach of the Code as it did not state clearly that celecoxib was not licensed and was very vague about expected costs and budgetary implications. The Panel noted that the information supplied by the companies with regard to advance information consisted of the four booklets, Celecoxib Clinical and Budgetary Information, The Burden of Arthritis, COX-1 and COX-2 and The Ageing Population. The two medical information documents had not been used for this purpose.

The two medical information documents had been sent in response to individual requests for information. The Panel noted that replies made in response to individual enquiries were excluded from the definition of promotion if they related solely to the subject matter of the enquiry, were accurate and not misleading and were not promotional in nature. The Panel considered that there was no complaint about the two medical information documents, they were not part of the advance product information. The Panel did not therefore review these documents.

The Panel was unsure how the intended audience, directors of public health and pharmaceutical and medical advisers, learnt about the forthcoming product. The letter from Searle stated that the NHS liaison team used the documents with the intended audience after determining the audience's wish to receive information. If the audience had asked Searle and/or Pfizer for information then the Code would not apply if the request was unsolicited. It appeared that the companies initiated discussions with the intended audience and then provided the four documents. This was a solicited request and not exempt from the Code. As the budgetary implications had been raised by Searle and Pfizer the information had to comply with the requirements of the supplementary information to Clause 3.1.

The Panel noted the intended audience, directors of public health and pharmaceutical and medical advisers. The Panel queried whether pharmaceutical and medical advisers would be responsible for making policy decisions on medicines in health authorities and trust hospitals and the like as required by the supplementary information to Clause 3.1. The Panel was concerned that the material had been sent to prescribing advisers to primary care groups given

that the supplementary information referred to health authorities and trust hospitals etc. The Panel accepted that the supplementary information had been agreed prior to the introduction of primary care groups.

The Panel examined the four booklets in detail. The booklet Celecoxib Clinical and Budgetary Information first gave an overview of the clinical data and then referred to the budgetary implications. The relevant two pages included a chart which gave the ranges of the costs of NSAIDs (£1.44 – £19.40) and the associated add on costs such as treatment with H2 antagonists and proton pump inhibitors (£8.55 – £32.28), the range for the cost of analgesics (£1.08 – £20.64) and the associated add on costs such as laxatives (£4.24 – £12.86). In each case, however, there was no indication as to the proportion of patients who received an expensive NSAID or analgesic or the proportion who would need H_2 antagonists or laxatives. The chart also gave a range for the cost of celecoxib as between £10 and £29 for 30 days' treatment. The second page included a chart headed 'Potential Budgetary Implications'. This listed the potential savings as less use of co-prescriptions eg gastro protectants, reduction in secondary care costs eg serious GI events and savings in the social services budget. The potential costs were listed as switches from generics to celecoxib. The switch from branded NSAIDs was positioned in such a way as to give the impression that this would be cost neutral. There would be potential savings and potential costs.

The booklet The Burden of Arthritis gave details of the cost of the disease and its treatments. There were no indications of the costs or savings of switching patients to celecoxib.

The Panel noted that the exemption for advance information related to the introduction of new medicines or changes to existing medicines which might significantly affect health authorities' and trust hospitals' level of expenditure during future years. The Panel did not know whether the introduction of celecoxib would significantly affect expenditure in future years because the material did not make this clear. In this regard the Panel noted that the materials did not give sufficient information to enable the reader to determine whether the use of celecoxib to treat arthritis would require more money overall or less money overall. In the Panel's view the companies had not demonstrated that the introduction of celecoxib might significantly affect levels of expenditure in future years. The materials did not explore this in any detail. In the Panel's view therefore the materials should not have been issued at all. The Panel ruled a breach of Clause 3.1 of the Code.

The Panel agreed with the companies that it was not a specific requirement of the Code to state that the product was not licensed in the UK. In the Panel's view, however, it would have been helpful if this information had been given in the material.

APPEAL BY SEARLE AND PFIZER

Searle appealed on behalf of both companies and addressed the issues of the content and the use of the material separately.

1 Use of the advance information on celecoxib

'The Panel was unsure how the intended audience, directors of public health and pharmaceutical and medical advisers, learnt about the forthcoming product'.

Searle stated that its and Pfizer's managed entry teams, which were the companies' NHS liaison personnel, were briefed that, during the pre-launch period, they could only initiate discussions on the budgetary implications of celecoxib with NHS managers with budgetary policy responsibilities. The types of role that were identified as falling within this remit were directors of public health, pharmaceutical advisers, medical advisers, chief executives, directors of finance, primary care group (PCG) managers, GP commissioning managers and directors in primary care. Part of the managed entry teams' remit had been to identify the appropriate individuals and confirm their need and wish to receive advance information on celecoxib. Discussions were then initiated by Searle and Pfizer with the relevant audience and complied with Clause 3.1. Searle noted that in addition to the discussions initiated by the companies they had received several direct requests from NHS managers for information on the product and its financial implications. On the occasions the companies had been approached, information had been provided by the medical department or the managed entry team according to the enquirer's preference. This was indicative of the considerable NHS management interest in this area and, in that regard, both the National Prescribing Centre and the Pharmacy Practice Division in Scotland had already issued bulletins on celecoxib and the companies had received preliminary notification that the product was proposed for appraisal by the National Institute of Clinical Excellence (NICE).

Searle stated that it was clear, therefore, that the NHS regarded the introduction of products such as celecoxib as having a (potentially) significant impact on the health service, including its budgets.

'The Panel queried whether pharmaceutical and medical advisers would be responsible for making policy decisions on medicines in health authorities and trust hospital and the like…. The Panel was concerned that the material had been sent to prescribing advisers to primary care groups given that the supplementary information referred to health authorities and trust hospital etc. The Panel accepted that the supplementary information had been agreed prior to the introduction of primary care groups.'

Searle stated that it was surprised that the Panel had queried the responsibility of pharmaceutical and medical advisers in making policy decisions in health authorities etc. Their role was integral to the development of policies on the use of and expenditure on new medicines. Pharmaceutical advisers, in particular, were responsible for managing the introduction and financial implications of new medicines and whilst no one individual was solely responsible for decisions on budget, in some health authorities the pharmaceutical adviser was identified as the key person who needed to receive and evaluate information on new medicines. A letter from a health

authority pharmaceutical adviser which clearly demonstrated their role and need for information was provided.

Searle also noted the Panel's concern that material had been sent to prescribing advisers to PCGs but would point out that the supplementary information to Clause 3.1 read 'Health authorities and trust hospitals etc need to estimate their likely budgets…' and clearly the list of appropriate bodies was not intended to be exhaustive. As the Panel noted, the supplementary information was agreed prior to the introduction of PCGs. The companies' view was that it would be inappropriate to deny PCGs advance product information when their interest in, and need for such information, was clear and proper (as they too had to estimate budgets), simply because the current edition of the Code had not caught up with the changes in the structure of the NHS. In any event the companies considered that the function of PCGs meant that they were covered by the 'etc' referred to in the current supplementary information.

Searle noted that the role of PCGs was still developing and evolving but many of them were 'Level two' with devolved responsibility for commissioning and budgets. Many groups had already applied for 'Level three' status when they would be responsible for purchasing all care for their patients. As with health authorities and trust hospitals, they needed to estimate their likely budgets. Whilst the companies had not approached Level 1 PCGs they had included Level 2 budget holders in their discussions on the financial impact of celecoxib, as the vast majority of the arthritis patient population was chiefly managed within the primary care environment. The companies thus considered it was entirely appropriate to approach the PCG prescribing advisers with budgetary responsibility.

2 Content of advance information material

'The Panel did not know whether the introduction of celecoxib would significantly affect expenditure in future years because the material did not make this clear. In this regard the Panel noted that the materials did not give sufficient information to enable the reader to determine whether the use of celecoxib to treat arthritis would require more money overall or less money overall. In the Panel's view the companies had not demonstrated that the introduction of celecoxib might significantly affect levels of expenditure in future years. The materials did not explore this in any detail. In the Panel's view therefore, the materials should not have been issued at all.'

Searle noted that the Panel's view that the material should not have been issued was based on the premise that the companies did not demonstrate that celecoxib's introduction would significantly affect levels of expenditure, and that they did not indicate whether the use of celecoxib would require more or less money overall. On the latter point the companies argued, very strongly, that if the introduction of a product could result in significant changes to expenditure in different areas (such as an increase in medicine costs and a decrease in hospitalisation costs) then this had important budgetary implications for those responsible for budgetary planning and policy decisions, even if the overall effect was cost neutral. This was an important principle and Searle and Pfizer did not consider that the supplementary information to Clause 3.1 indicated that the overall impact of a new product or product change must be an increase or decrease in costs.

Searle noted that the Panel noted that in the booklet Celecoxib Clinical and Budgetary Information the range of costs for NSAIDs, analgesics and add-on therapy costs were given but that … 'in each case, however there was no indication as to the proportion of patients who received as expensive NSAID or analgesic or the proportion who would need H2 antagonists or laxatives…'.

The introductory booklet The Burden of Arthritis gave more information on the overall UK situation with the number of prescriptions (and overall cost) for NSAIDs and analgesics. It also stated that '10% of NSAID users are prescribed a concurrent gastroprotective agent' and 'in a recent survey 26% of patients taking stronger analgesics required co-prescription of laxatives'. Thus, although this information was not presented in the booklet Celecoxib Clinical and Budgetary Information, the available information on co-prescription was presented along with other data on the current costs of managing arthritis.

There was no data presented in any of the booklets as to the proportion of patients who required an expensive NSAID or an analgesic as Searle and Pfizer did not consider this level of detail to be either necessary or helpful to the audience. There were local policies in place throughout the UK with regard to NSAID and analgesic use and the recommendations for co-prescriptions were often encompassed by local protocols. The recent recommendation from one health authority was that first line therapy for 'at risk' patients who required an NSAID was high-dose ibuprofen and generic cimetidine; this was different from the recommendations in other authorities.

Searle stated that this variation in local practice was one of the primary reasons that the advance information on celecoxib did not prescribe the financial impact of celecoxib for the budget holder audience. The Panel's view was that not sufficient information had been given in the material to determine the effect on expenditure. Searle submitted that as the purpose of advance notification was to provide information for health authorities etc to estimate and plan their future budgets, the information provided on costs and budgetary implications was appropriate and sufficient for this purpose.

Searle noted that one page of the booklet Celecoxib Clinical and Budgetary Information laid out the areas where the companies considered that the use of celecoxib might result in potential savings and costs. The companies could have provided scenarios based on assumptions about the patients celecoxib would be used in, the therapies it would replace etc and calculated the actual financial impact. In the companies' view this was not appropriate and would be disingenuous; whilst they could and should

provide the appropriate data on the clinical profile, costs and potential budgetary implications of the introduction of celecoxib, the health authorities etc would determine the role the product would play in the management of their patients and hence the actual budgetary impact.

Lastly, as mentioned in its original submission, Searle noted that the MCA did not regard the company's material as breaching Regulation 3(1) of the Medicines (Advertising) Regulations 1994 (as amended). This fact clearly supported the company's contention that there was no breach of Clause 3.1 of the Code. The basis for this contention was that both provisions were aimed at the same harm, namely the advertising/promotion of a medicine before a marketing authorization had been granted. The MCA's (draft) guidance on this prohibition was broadly the same as the supplementary information to Clause 3.1 of the Code, stating as follows:

'Companies can disseminate limited factual information to persons such as health authority or trust hospital budget holders where that information may be significant to the planning of their expenditure over future years, for example for novel medicines or new means of administration where the changes may have significant cost implications. The information should be targeted at those who need to make budgetary decisions rather than to prescribers.'

The 'rules' on the provision of advance information on new, unlicensed products were therefore common to both the Regulations and the Code. Searle had explained above the reasons for its belief that the material (including the way it was used) had been in compliance with these rules and it appeared that the MCA's decision, that the companies had committed no breach of Regulation 3(1) (presumably including the guidance referred to above), supported that view.

In summary therefore the companies considered that the material and its use in the advance notification of celecoxib complied with the letter and spirit of Clause 3.1 of the Code and the supplementary information.

APPEAL BOARD RULING

The Appeal Board noted that Clause 3.1 of the Code prohibited the promotion of a medicine prior to the grant of the marketing authorization. Clause 3.1 reflected the legal requirements in the UK. The relevant supplementary information to Clause 3.1 provided a limited exemption to that prohibition and permitted companies to provide advance notification only in relation to products which might significantly affect levels of expenditure. The supplementary information also set out limitations on the use of advance notification. There was no similar exemption to UK legal requirements. The guidelines referred to by Searle and Pfizer in their submission were draft guidelines and had not yet been issued by the MCA.

The Appeal Board noted the comments made by the Panel about the roles of medical and pharmaceutical advisers and prescribing advisers to primary care groups. The Appeal Board considered that it was appropriate to provide advance information to medical and pharmaceutical advisers and to prescribing advisers in primary care groups. The supplementary information should be updated to make this clear.

The Appeal Board considered that with regard to advance notification it would be helpful to state clearly that the product concerned was not yet licensed. This was not a requirement of the Code but the Appeal Board recommended that it should be added to the supplementary information to Clause 3.1 when the Code was next updated.

The Appeal Board appreciated the need of the NHS to receive information about products prior to them reaching the market. However, the promotion of unlicensed products or unlicensed indications would be a breach of Clause 3.1 of the Code. The exemption in the supplementary information to Clause 3.1 was limited to products which might significantly affect levels of expenditure. Further detail was provided in paragraph (iii) of the supplementary information which stated that the likely cost and the budgetary implications must be indicated and must be such that they would make significant differences to the likely expenditure of health authorities, trust hospitals and the like.

Turning to the case now before it, the Appeal Board accepted the difficulties of establishing the price of a medicine before it was launched. The Appeal Board considered that Searle and Pfizer had not demonstrated that the introduction of celecoxib might significantly affect levels of expenditure in future years. The materials did not explore this in sufficient detail. The Appeal Board therefore upheld the Panel's ruling of a breach of Clause 3.1 of the Code.

The appeal was thus unsuccessful.

Complaint received **19 July 1999**

Case completed **9 November 1999**

GENERAL PRACTITIONER v JANSSEN-CILAG

Sporanox-Pulse journal advertisement

A general practitioner complained about a journal advertisement for Sporanox-Pulse (itraconazole) issued by Janssen-Cilag. The complainant alleged that the advertisement was misleading because it gave the general impression that Sporanox-Pulse was a very effective treatment of fungal foot infections whereas a recently published clinical study showed that better response rates were achieved with terbinafine.

The Panel noted that the advertisement promoted Sporanox-Pulse for use in fungal foot infections generally. Readers were informed that if they did not know which fungus was causing a patient's foot infection, Sporanox-Pulse was likely to be effective. The clinical study referred to by the complainant had compared Sporanox-Pulse with terbinafine in patients with dermatophytic infection of the toenail ie a sub-section of the patient population for which the product was being promoted. The Panel did not consider that the advertisement was misleading as alleged and ruled no breach of the Code.

A general practitioner complained about an advertisement (ref 0649E) for Sporanox-Pulse (itraconazole 400mg a day for one week in every four) issued by Janssen-Cilag Ltd. The advertisement had appeared in Doctor, 3 June 1999, and featured two trainer shoes having a whimsical conversation. One trainer was saying to the other 'If he doesn't get Sporanox-Pulse this time, I'll do a runner'. Underneath, in a box of text was the statement 'If you were in their shoes, wouldn't you kick up a fuss? After all, Sporanox-Pulse is very broad spectrum. It can tackle both dermatophytes and yeasts. And if you're not sure which fungus is causing the problem, it's pretty sure to do the trick.' The strapline, which appeared at the bottom of the box of text, read 'Foot therapy that's hard to fault.'

COMPLAINT

The complainant stated that the general impression given by the advertisement was that Sporanox-Pulse was a very effective treatment for fungal foot infections and that the owner of a fungally infected foot would be justified in feeling hard done by if Sporanox-Pulse was not prescribed.

The complainant stated that in April 1999, a paper published in the BMJ reported the findings of a large well designed study – the LION study. This study compared itraconazole (Sporanox-Pulse) with terbinafine (Lamisil) in the treatment of fungal foot infections. It involved nearly 500 patients and showed that the response rate on itraconazole was 38% and 49% compared with 76% and 81% on terbinafine – depending on the length of the treatment period (Evans and Sigurgeirsson (1999)).

The complainant stated that it was difficult to imagine that this paper had escaped the attention of Janssen-Cilag. Nevertheless the advertisement, claiming that Sporanox-Pulse was 'Foot therapy that's hard to fault' was issued. This seemed a little hollow in the face of the published data. Indeed a 38% vs 76% chance of a mycological cure at 3 months or a 49% vs 81% chance at four months would indicate that the trainers should have done a runner if the GP did prescribe Sporanox-Pulse. In short, treatment with Sporanox-Pulse was not hard to fault because a better alternative was available.

In summary the complainant alleged that the advertisement was highly misleading because it suggested that an outmoded and relatively ineffective treatment was the best that was available.

RESPONSE

Janssen-Cilag noted that the complainant referred to the LION (Lamisil (terbinafine) versus itraconazole in onychomycosis) study as a study which had compared itraconazole with terbinafine in the treatment of fungal foot infections. The study, however, was much more circumscribed than this. The authors stated that 'the objective of [the study] was to compare the efficacy and safety of continuous terbinafine with intermittent itraconazole in the treatment of toenail onychomycosis.' Onychomycosis was defined in Dorland's Medical Dictionary as 'a disease of the nails of the fingers and toes caused by … several species of [dermatophytes] or by Candida'. Both dermatophytes and Candida (a yeast-like organism) species were types of fungus.

Janssen-Cilag noted that the advertisement in question did not make any specific claims as to the treatment of toenail disease, the problem which the LION study addressed. Rather the advertisement focused on the larger issue of fungal infections of the foot. Such infections included not only toenail onychomycosis but also the other major category of possible superficial fungal infections ie, those involving the skin (as opposed to the nails).

Janssen-Cilag noted that, in addition to its licence for the treatment of onychomycosis, Sporanox-Pulse was licensed for the treatment of tinea pedis (athlete's foot). Terbinafine was also licensed for the treatment of tinea pedis; however, Janssen-Cilag was unaware that terbinafine had been shown to have any advantage over itraconazole (Sporanox-Pulse) in the treatment of this condition. Thus the company considered that it was justified in making the claim in the overall disease area of fungal foot infections that Sporanox-Pulse offered 'Foot therapy that's hard to fault'.

Janssen-Cilag stated that with regard to fungal nail infections, it should be emphasised that the cause of onychomycosis was not merely dermatophytic fungi, but that causative organisms could come from another part of the fungi family, ie – from the yeast group, in the form of various Candida species. Sporanox-Pulse

had as one of its therapeutic indications the treatment of onychomycosis, whether caused by dermatophytes and/or yeasts. Terbinafine, however, had no spectrum of activity against members of the yeast branch of the fungi family in so far as fungal infections of the nail were concerned; its indications in this area only included dermatophyte infections of the nails.

Janssen-Cilag stated that as doctors might not always go to the trouble of obtaining a nail cutting for analysis of the causative agent in a case of suspected onychomycosis, or might not wish to await the results of any such analysis of a cutting before beginning treatment (ie, initial blind treatment with an antifungal agent), a tactical decision to use a broad-spectrum anti-fungal agent such as Sporanox-Pulse (which acted against both dermatophytes and yeasts in nail disease) might be taken. In like fashion, in tinea pedis, 'the infections may spread to adjacent areas of the foot, including the toenails … [and] concomitant mould, candidal and/or bacterial infection is relatively common in patients with tinea pedis.' (Richardson & Warnock (1997)). Thus, again, a broad spectrum approach to treatment might be useful. Such an approach was suggested by the Sporanox-Pulse advertisement, which stated: 'After all, Sporanox-Pulse is very broad spectrum. It can tackle both dermatophytes and yeasts. And if you're not sure which fungus is causing the problem, it's pretty sure to do the trick.'

Janssen-Cilag made a number of comments about the LION study. The study compared continuous terbinafine with intermittent itraconazole in patients with toenail infections caused only by dermatophytes. The study population appeared to be unrepresentative of the usual patient seeking treatment for onychomycosis. The introduction to the paper cited a prevalence rate amongst adults of 2-4%. Janssen-Cilag considered the patient population in the LION study to have severe onychomycosis (on average a 10-year history with six toenails affected). No evidence was adduced by which one could demonstrate the relevance of this study to a wider population of patients with mild or moderate onychomycosis.

Janssen-Cilag stated that the results of the LION study were not representative of the overall meta-analysis of clinical trials that demonstrated comparable efficacy between continuous terbinafine and intermittent itraconazole (Gupta and Lambert (1999)). The meta-analysis, which included the clinical response and mycological cure rates from open, placebo controlled and comparative studies (including the LION study), suggested similar efficacy rates between itraconazole pulse therapy and terbinafine continuous therapy for the treatment of dermatophyte toenail onychomycosis. The meta-analysis reported mycological cure rates of itraconazole (pulse) as 73.6%±5.5% (95% confidence intervals, CI, 62.8% to 84.3%, 1596 patients, 12 studies) and terbinafine 78.8%±4.0 (95% CI, 71.1% to 86.6%, 1355 patients, 18 studies). The corresponding clinical response rates were itraconazole (pulse) 85.1%±3.2% (95% CI, 78.9% to 91.4%, 1207 patients, 8 studies) and terbinafine 84.0%±4.2% (95% CI, 75.9% to 92.2%, 588 patients, 7 studies).

Janssen-Cilag stated that several independent studies, that had not been included in the meta-analysis, had either been recently presented or published and provided further support for the results of the meta-analysis. One such study, Negroni *et al* (1998), involved 228 evaluable patients (117 in the intraconazole pulse group and 111 in the terbinafine group). The study demonstrated a 71% effective cure (mycological cure plus clinical response of >75% of the affected nail) for the itraconazole pulse group and 53.1% in the terbinafine group. In a study by Bahandir *et al* (1998) 65.2% patients on itraconazole (n=25) and 70.5% of those on terbinafine (n=35) were considered clinically and mycologically cured. Finally, Kejda *et al* (1999) reported mycological cure rates of 75% in the itraconazole pulse patients (n=26) and 76% in the terbinafine group (n=25). The corresponding clinical cure rates were 77% and 68%, respectively. Similarly, in dermatophyte skin and fingernail infections, comparative trials between itraconazole (pulse) and terbinafine showed comparable results.

Janssen-Cilag stated that although there might be differences in clinical and mycological cure rates from study to study, the results of the LION trial were discordant with the wealth of clinical results that had been documented in the literature.

Janssen-Cilag stated that it had evaluated the LION study before publishing the advertisement for Sporanox-Pulse and had also conducted further literature searches in order to assure itself that any claims made by the promotion would be accurate, balanced, fair, objective and unambiguous. The claim that Sporanox-Pulse's broad spectrum of activity was an asset for effective treatment of fungal foot infections was founded upon evidence-based medicine and within the provisions of Clause 7.2 of the Code.

PANEL RULING

The Panel noted that the advertisement promoted Sporanox-Pulse for use in fungal foot infections generally. The advertisement referred to the product's broad spectrum of activity in that it was effective against both dermatophytes and yeasts; readers were informed that even if they did not know which fungus was causing a patient's foot infection, Sporanox-Pulse was likely to be effective. There was no actual or implied comparison with terbinafine therapy. The prescribing information stated that Sporanox-Pulse was for use in onychomycosis, tinea pedis and/or tinea manuum.

The LION study had compared Sporanox-Pulse with terbinafine in a very specific patient group ie those with dermatophytic infection of the toenails. Thus the patient population in the LION study would represent only a sub-section of that for which Sporanox-Pulse was being promoted. The Panel noted the data referred to by Janssen-Cilag. The Panel did not consider that the advertisement was misleading as alleged and ruled no breach of Clause 7.2 of the Code.

Complaint received **20 August 1999**

Case completed **15 October 1999**

GENERAL PRACTITIONER v ASTRAZENECA

Sponsorship of meeting

A general practitioner complained that AstraZeneca could spend what she thought was an unacceptable amount of money offering general practitioners a fairly unexciting two day meeting at a Cambridge College.

The Panel noted that the meeting started with lunch one day and finished with lunch the next. The Panel considered that in between time the educational content of the meeting was not unreasonable and the hospitality had not been out of proportion to the occasion. The costs incurred for the meeting were not unreasonable and no breach of the Code was ruled.

A general practitioner complained about an invitation to a meeting entitled 'Dispensing – Towards the Millennium', held at a Cambridge College, and sponsored by AstraZeneca.

COMPLAINT

The complainant stated that she was amazed when one considered the cost of medicines to the National Health Service that it could be acceptable that AstraZeneca could spend what must be a considerable amount of money offering general practitioners what the complainant considered a fairly unexciting programme. The complainant was sure that the cost of putting on a programme which covered two days at a Cambridge College, offering a reception in the evening and a meal, accommodation and travel by air or rail or car, was unacceptable.

When writing to AstraZeneca the Authority invited it to consider the requirements of Clause 19 of the Code.

RESPONSE

AstraZeneca stated that the meeting was the third of its kind which it had organised specifically for dispensing doctors in the last twelve months. The previous meeting was held at a different Cambridge College in March 1999. Following the meeting in March, AstraZeneca conducted a focus group meeting of dispensing GPs and the message which it received from that was that the meeting was very educational and valuable and that the content and format should not be changed. The meeting in March was over-subscribed. One hundred and one doctors attended and a further fifty-one elected to go on a waiting list for the next meeting (ie the meeting at issue). The programme content for the meeting at issue was similar to that for the meeting held in March and the meeting had been awarded 7 hours PGEA approval (3 hours clinical and 4 hours service management).

AstraZeneca was, therefore, satisfied that the meeting was educational and of interest to dispensing doctors. The appeal of any particular meeting was, of course, a matter of personal interest and taste. AstraZeneca was disappointed that the complainant considered the programme to be fairly unexciting. However, this was clearly not a view shared by a great many dispensing doctors for whom the meeting had been organised.

With regard to the cost of the meeting, it might be that certain assumptions had been made on the part of the complainant. Accommodation for the delegates was the student accommodation at the College, and this was reflected in the cost. Copies of the invoices were provided. The cost of 52 delegates, 7 speakers and 8 AstraZeneca staff was £9627.15 (giving a figure of £143.69 per person).

With regard to travel arrangements, delegates were normally expected to travel by car or train. Only in exceptional circumstances was air travel offered eg where distances were such that travel by car or train was impracticable. Details of the travel costs were provided.

A copy of the programme for the meeting at issue was provided and this also contained the acceptance form to be completed by the delegate. Invitations to the meeting had been extended to dispensing doctors either personally by the local AstraZeneca account managers or by AstraZeneca's postgraduate education manager.

AstraZeneca stated that in meetings of this kind, it was normal practice to ask delegates to complete an evaluation form. The reason for asking delegates to provide anonymous comments on the meeting and suggestions for future meetings was to assist the company in providing high quality meetings on subjects of interest and value to delegates. Copies of the 38 evaluation forms which were returned were provided. Consistently high scores were given for the quality of the speakers and the relevance of the subject matter. Not one gave a low score for these.

Furthermore, a number of favourable comments were made on the excellence of the organisation of the meeting and on the educational value eg *'An excellent meeting. The best PGEA I have attended!'*. Only one comment on the accommodation was received – *'…the accommodation, though frugal was adequate'*. Finally, delegates were also asked on the form whether any sponsorship of the meeting was intrusive. All 38 delegates returning forms answered *'No'* and one delegate commented *'…a refreshingly unbiased approach towards any particular companies (sic) interest'*.

In conclusion, AstraZeneca submitted that the meeting was educational and of interest and value to dispensing doctors. It also submitted that the cost of the meeting was considerably less than that which might be anticipated from hotels at which doctors might expect to stay. In AstraZeneca's view, the hospitality associated with the meeting was secondary to the purpose of the meeting and the costs involved were no greater than that which delegates might normally pay for themselves. AstraZeneca was firmly

of the belief that the arrangements for this meeting were entirely consistent with all the requirements of the Code, including Clause 19.

PANEL RULING

The Panel noted that Clause 19.1 of the Code permitted companies to provide appropriate hospitality to members of the health professions and appropriate administrative staff in association with scientific and promotional meetings, scientific congresses and other such meetings. Hospitality must be secondary to the purpose of the meeting and the level of hospitality offered must be appropriate and not out of proportion to the occasion.

When considering whether a meeting and associated hospitality contravened the Code all the circumstances had to be considered including cost, location, educational content, level of hospitality and the overall impression created by the arrangements. Each case had to be considered on its own merits. In the Panel's view the programme should attract delegates and not the venue.

The Panel noted that the meeting started with lunch on the Thursday. The educational programme started at 2pm and finished with the Chairman's summary at 5.15pm. A modest dinner, with wine, had been provided in the evening. The educational programme continued at 9am on the next day finishing at 1pm with lunch. The programme covered treatment of asthma and migraine as well as clinical governance and non-verbal communication. The Panel considered that the educational content was not unreasonable and the hospitality had not been out of proportion to the occasion.

The invitation stated that the meeting was supported by an educational grant from AstraZeneca. Delegates were asked about travel arrangements. AstraZeneca would provide rail/air tickets if required.

The Panel noted that the cost of overnight accommodation, meals, conference facilities etc came to just under £144 per head. Travel was not included.

The Panel noted the forms completed by the participants were complimentary about the educational part of the meeting.

The Panel accepted that the cost of the meeting at £144 plus travel expenses might be seen as exceeding the level that some recipients would normally adopt when paying for themselves. In the Panel's view however the costs were not unreasonable. The meeting was acceptable and no breach of Clause 19.1 of the Code was ruled.

Complaint received **20 August 1999**

Case completed **21 October 1999**

CASE AUTH/915/8/99

SANOFI WINTHROP v SCHWARZ PHARMA

Tylex advertisement

Sanofi Winthrop complained about a claim 'In an independent study, three times as many patients favoured the blackcurrant taste of Tylex Effervescent to an alternative effervescent formulation' in an advertisement for Tylex issued by Schwarz Pharma.

Sanofi Winthrop pointed out that the study to which the claim was referenced was carried out in healthy volunteers. The Panel considered that the claim was inaccurate and misleading as the study had not been carried out on patients. A breach of the Code was ruled.

Sanofi Winthrop further alleged that to use a study in 12 healthy male volunteers aged 18-40 to make claims about taste preference in a mixed population of patients suffering pain was inappropriate and not relevant to the clinical situation. The Panel noted that the extrapolation of healthy volunteer data to the clinical situation should only be made where there was data to show that it was of direct relevance and significance. The study was a healthy volunteer study and it was too small to be extrapolated to all patients. The Panel ruled that the claim was exaggerated and misleading in breach of the Code. Upon appeal by Schwarz, the Appeal Board considered that it was inappropriate to extrapolate the results obtained in a small, single dose, open label study to an entire population of patients, many of whom would require the medicine on a chronic basis. The Panel's rulings were upheld.

Sanofi Winthrop Limited complained about an advertisement for Tylex (co-codamol 30/500) issued by Schwarz Pharma Limited (ref 1149). The advertisement featured the heading 'Kill it in the best possible taste' together with the claim 'In an independent study, three times as many patients favoured the blackcurrant taste of Tylex Effervescent to an alternative effervescent formulation'. The claim at issue was referenced to 'Data on file at Schwarz Pharma Limited – Study no: T0105'. The alternative effervescent formulation with which Tylex had been compared was Sanofi Winthrop's product Solpadol Effervescent.

1 Use of the term 'patients'

COMPLAINT

Sanofi Winthrop noted that the claim at issue was referenced to 'Data on file at Schwarz Pharma Limited – Study no: T0105' A synopsis of the study was provided. Sanofi Winthrop stated that the study was carried out in healthy volunteers, not patients, therefore the claim was clearly inaccurate and misleading. A breach of Clause 7.2 was alleged.

RESPONSE

Schwarz stated that each of the healthy volunteers was asked to state a preference for the taste of two effervescent formulations, Tylex Effervescent tablets or an alternative co-codamol 30/500 effervescent formulation. Nine out of 12 subjects stated a preference for the blackcurrant flavour of Tylex Effervescent. Schwarz was unaware of any data to suggest that pain altered the taste preference of a patient and therefore considered it was reasonable to extrapolate the preferences of volunteers to those of patients, and hence used the term patient rather than volunteer in this advertisement. In view of this the company did not consider that this claim was in breach of Clause 7.2.

PANEL RULING

The Panel noted that the supplementary information to Clause 7.2, 'the use of data derived from *in-vitro* studies, studies in healthy volunteers and in animals', stated that care must be taken with such data so as not to mislead as to its significance. The extrapolation of such data to the clinical situation should only be made where there was data to show that it was of direct relevance and significance.

The Panel noted that study T0105 was a healthy volunteer study which showed that three times as many subjects favoured the taste of Tylex Effervescent compared with the taste of Solpadol Effervescent. The claim at issue, however, implied that the study had been carried out in patients which it had not. The Panel considered that the claim was inaccurate and misleading as alleged and a breach of Clause 7.2 was ruled.

2 Extrapolation of data

COMPLAINT

Sanofi Winthrop stated that the use of study T0105, which was in twelve healthy, male volunteers aged 18-40, to make claims about taste preference in a mixed population of patients suffering pain was inappropriate and not relevant to the clinical situation. Sanofi Winthrop alleged that the citation of the study was in breach of Clauses 7.2 and 7.8 of the Code.

RESPONSE

Schwarz noted that there was concern that taste preference for patients suffering from pain was not relevant to their clinical situation. The company did not consider that there was evidence to support such a statement and therefore found it inappropriate to dismiss the findings of the study in relation to taste preference. Schwarz could not therefore concur with the complainant's belief that the citation of this study was in breach of Clauses 7.2 and 7.8.

PANEL RULING

The Panel noted that study T0105 had involved only 12 healthy male volunteers aged 18-40. The supplementary information to Clause 7.2 'the use of data derived from *in-vitro* studies, studies in healthy volunteers and in animals' stated that care must be taken with such data so as not to mislead as to its significance. The extrapolation of such data to the clinical situation should only be made where there was data to show that it was of direct relevance and significance. Study T0105 was a healthy volunteer study and, in addition, the Panel considered that it was too small to allow its results to be extrapolated to all patients, male, female, young and old. Given the data on which it was based the Panel considered that the claim was exaggerated and misleading as alleged. Breaches of Clauses 7.2 and 7.8 were ruled.

APPEAL BY SCHWARZ PHARMA

Schwarz noted that the unpublished study cited in the Tylex advertisement was conducted in healthy volunteers. Each subject was asked to state a preference for the taste of two effervescent formulations, Tylex Effervescent tablets or an alternative co-codamol 30/500 effervescent formulation. The study demonstrated that a greater number of subjects (9 out of 12) stated a preference for Tylex Effervescent formulation versus the alternative co-codamol 30/500 effervescent formulation.

Schwarz stated that taste preference was considered to be a non-clinical end-point. The company was not aware of any evidence that showed pain altered the taste preference of a patient and considered therefore that in this case the preference of volunteers would not differ from that of patients. Schwarz noted that Sanofi Winthrop did not accept that the results of study T0105 could be extrapolated to patients and seemed to consider that taste preference was irrelevant to the clinical pain situation. Both the co-codamol 30/500 effervescent formulations needed to be dissolved in approximately half a tumblerful of water. Given the volume of liquid that needed to be swallowed it would seem reasonable to consider the influence taste had on the preference for one or other of the products. Certainly the results of study T0105 demonstrated that subjects did prefer one of the effervescent formulations over the other based on the taste of the solution. As Schwarz considered it was reasonable for the findings of this study to be extrapolated to patients, taste preference would certainly seem relevant to the clinical situation.

Schwarz noted that the Panel seemed to consider it acceptable to extrapolate taste preference expressed by healthy volunteers to patients although they felt the sample size of T0105 (12 healthy volunteers) was too small to allow extrapolation to patients. In the study, subjects expressed a clear taste preference for Tylex effervescent and Schwarz would still argue that the use of the results of this data in the advertisement was not in breach of Clauses 7.2 and 7.8. Schwarz stated that it would therefore like to appeal against the Panel's decision.

APPEAL BOARD RULING

The Appeal Board noted that study T0105 was an open label, single dose study in 12 healthy male volunteers. The company accepted that there was no statistical analysis of the data as the study had been too small. The Appeal Board noted that the supplementary information to Clause 7.2 did not prohibit the use of results which were not statistically significant but did state that differences that did not reach statistical significance must not be presented in such a way as to mislead.

The Appeal Board noted that no data had been submitted regarding taste preference in male and female patients across all age groups or the effect that different types of pain might have on the perception of taste.

Given the limited data, the Appeal Board did not consider it appropriate to extrapolate the results obtained in a single dose, open label study in 12 healthy male volunteers to an entire population of patients, many of whom would require the medicine on a chronic basis. In the Appeal Board's view doctors would regard the very positive claim that three quarters of their patients would prefer the blackcurrant taste of Tylex Effervescent to an alternative effervescent formulation quite differently if they knew the data upon which it was based. The Appeal Board upheld the Panel's rulings of breaches of Clauses 7.2 and 7.8 of the Code.

The appeal was thus unsuccessful.

Complaint received **24 August 1999**

Case completed **14 October 1999**

CASE AUTH/918/8/99

PFIZER v SCHWARZ PHARMA

Viridal Duo press release

Pfizer complained about a Viridal Duo press release, issued by Schwarz Pharma, entitled 'Viridal Duo more effective treatment for ED [erectile dysfunction] than [Viagra] …'. The press release discussed the results of a study published in 1999 which compared the cost effectiveness of Viridal Duo and Viagra using a computer model.

Pfizer alleged that the study conclusion was flawed as the efficacy data used in the computer model were not representative of the published data for Viagra. It did not provide an accurate or balanced comparison of the two products, based on an up-to-date evaluation of all the evidence, nor did it reflect that evidence clearly. Also Schwarz had used the conclusion notwithstanding the various caveats in the paper.

The Panel noted that although the study had been independently published and peer reviewed, Schwarz's use of it for promotional purposes brought it within the scope of the Code. The study cited two clinical studies, both published in 1997, in support of Viagra and stated that only one of them, in men with broad spectrum erectile dysfunction, presented results in a form that allowed meaningful comparison with other ED treatments with response rates of 42% and 55% at doses of 50mg and 100mg respectively. These response rates, however, were in fact from the other clinical study which had been in men with severe erectile dysfunction. The Viagra summary of product characteristics (SPC) stated that the proportion of patients reporting improvement varied from 43% to 84% according to aetiology. A study, published in 1998, which appeared relevant to the economic model had reported response rates to Viagra of up to 69%, although this work had not been cited in the study at issue.

The study discussed in the press release was a preliminary pharmacoeconomic model which 'should be updated as more robust data become available'. The press release ended with 'This is a predictive model rather than a real life situation'. By contrast the press release began 'Viridal Duo is more clinically effective [than Viagra]' which in the Panel's view was a strong clinical claim based on preliminary economic data.

The Panel considered that the press release provided a misleading comparison of Viridal Duo and Viagra. A breach of the Code was ruled. The Panel considered that it was inappropriate for Schwarz to distribute copies of the study for promotional purposes and a further breach of the Code was ruled.

The Panel noted that the study stated that Viagra was contraindicated for ED with severe vasogenic aetiology. This was not a contraindication listed in the Viagra SPC. By using the study Schwarz was thus providing inaccurate information about Viagra. A breach of the Code was ruled.

COMPLAINT

Pfizer Limited complained about a Viridal Duo (intracavernosal alprostadil) press release, issued 5 August 1999 by Schwarz Pharma Limited. The press release discussed the results of a paper published in the Journal of Medical Economics (Plumb and Guest (1999)).

Pfizer noted that the headline of the press release was 'Viridal Duo more effective treatment for ED than oral sildenafil and intraurethral alprostadil'. The press release referred to the conclusion of a study, carried out on the basis of a computer model, that Viridal Duo was clinically more effective than sildenafil (Pfizer's product Viagra). A reprint of the published study, entitled 'Cost-effectiveness of Viridal Duo compared to MUSE and Viagra in the treatment of erectile dysfunction in the UK – a preliminary model', was provided to Pfizer upon request, which together with the press release clearly indicated that Schwarz was using it to promote Viridal Duo. The press release and the use of the published paper therefore clearly fell within the scope of the Code.

Pfizer alleged that the study conclusion was flawed and had been used in an inappropriate and misleading way, not least because the efficacy (response rates) data used in the computer model were not representative of the published data for Viagra. It did not therefore provide an accurate or balanced comparison of the two products, based on an up-to-date evaluation of all the evidence, nor did it reflect that evidence clearly. Also, in the press release Schwarz had used this conclusion notwithstanding the various caveats in the paper (see below). Pfizer alleged that the press release breached Clause 7.2 of the Code.

In particular, the response rate quoted in the study for Viridal Duo (defined as an erection of rigidity for intercourse) was 'between 60% and 80% across all aetiologies'. In relation to Viagra it was stated that 'only one study presented results in a form that allowed meaningful comparisons with other ED [erectile dysfunction] treatments'. The grounds for this statement were not made clear and it was particularly questionable in view of the fact that the study was referenced incorrectly; in any event there had existed for some time various other published data which were not referred to here. The response rates quoted for Viagra were 42% and 55% at the 50mg and 100mg doses respectively. These figures were taken from a single six month study in men with ED (Steers *et al* (1997a)). However, the figures quoted were not from this study. Rather, they were found in the report of a different study (Steers *et al* (1997b)). It was key to note that this study (Steers (1997b)), from which the efficacy figures were actually taken, albeit from the same authors and presented at the same meeting in October 1997, was in men with severe erectile dysfunction.

The Viagra efficacy figures were thus taken from a single study reported almost two years ago concerning a severely affected patient population in which response rates would be expected to be lower than in a more general population of ED patients. The response rates for Viridal Duo were derived, as far as Pfizer knew, from studies in patients with varying degrees of ED. Pfizer did not have copies of the full papers referred to in substantiation of the Viridal Duo response rates, but the abstract published on the Internet for one of them, Purvis *et al* (1996), referred to the varying response levels of the patients studied, stating that the combination of increasing age and anti-hypertensive medication and, in general, a reduced incidence of morning erections, were both predictive for a weaker response to alprostadil.

Pfizer stated that the data used as the basis for the response rates for Viridal Duo and Viagra did not compare like with like, in that the Viagra response rates were derived from only one study in men with severe ED, whilst the Viridal figures related to studies in populations of patients with ED of varying degrees. Being the data on which the computer model's conclusion was based, the use of it by Schwarz in the press release (or otherwise) amounted to an inaccurate, unbalanced and unfair comparison of the two products. Moreover, it did not reflect either the summary of product characteristics (SPC) for Viagra, which referred to clinical trials of sildenafil in more than 3,000 patients of varying ages and aetiologies and efficacy rates across all trials and all doses from 43% to 84%. The rate in mixed ED was given as 77%. Neither did the figures used in the article reflect all the published data available on the efficacy of sildenafil, Goldstein *et al* (1998) reported a response rate of 69%, that was 69% of all attempts at sexual intercourse were successful in patients treated with sildenafil.

Pfizer stated that furthermore, the incorrect reference would lead readers who consulted the list of references at the end of the study to believe that the figures were derived from a more general study of the long-term efficacy and safety of sildenafil rather than the study in patients with severe ED which, as explained above, was the true source of the data. This compounded the misleading effect of the study's conclusions.

Pfizer stated that there was another misleading reference to Viagra where it was stated that treatment with Viagra 'is contraindicated for ED with severe vasogenic aetiology'. This was incorrect and did not accurately reflect the SPC.

Pfizer stated that as referred to above, Schwarz's use in the press release of the conclusion of the study without reference to its acknowledged limitations was also misleading. For example it was stated in the study that '… the actual probability of successful treatment with Viagra is uncertain due to a lack of available comparable data'. Although Pfizer did not agree with this statement and did not know the basis on which it was made, the company would agree with the following sentence which read: 'Therefore Viridal Duo's cost effectiveness relative to Viagra may be an under- or over-estimate and should be treated with caution until further information becomes available.'

Also, the final sentence of the conclusion of the study which stated: 'However, these results should be updated as more robust data become available.'

Pfizer contended that more appropriate and accurate efficacy data for Viagra were definitely available and alleged that the promotional use by Schwarz of the conclusions of the paper therefore breached Clause 7.2 of the Code.

RESPONSE

Schwarz noted that the study in question compared the cost-effectiveness of three treatments for erectile dysfunction, Viridal Duo, MUSE and Viagra, using a preliminary pharmacoeconomic model; it had been published in a peer reviewed journal and therefore had been subjected to the scrutiny of several experts within the field of medical economics.

Schwarz noted that Pfizer considered that the study results had been used in an inappropriate and misleading way because the efficacy (response rates) used in the computer model were not representative of the published data available for Viagra and therefore the press release breached Clause 7.2 of the Code. The complaint focused on the discussion of efficacy (response rate) data presented for Viridal Duo and Viagra in the introduction of the study and did not mention the extensive methodology details presented in a later part of the study. Pfizer wrongly considered that it was only the data discussed in the introduction that was included in the pharmacoeconomic model. Schwarz referred to the methodology section 'Clinical outcomes and resource utilisation' that described the method of obtaining estimates of clinical outcomes used for the model. This clearly stated that the clinical outcomes were obtained from published literature and interviews with a Delphi panel using a modified Delphi technique. Thus, efficacy data relating to each product available at that time was reviewed by the panel and considered alongside their own clinical experience. A subsequent meeting of experts then agreed on the final estimates of clinical outcomes, treatment pathways and resource use to be used in the pharmacoeconomic model as presented in summary in the article.

A study by Porst (1997) was used to establish the relative cost-effectiveness of Viridal Duo in the management of ED. The study population was men with chronic ED. Pfizer's assertion that the response rates relating to Viridal Duo were derived from studies in patients with varying degrees of ED was therefore incorrect.

Schwarz stated that a range of efficacy data pertaining to Viagra was presented to the Delphi panel for assessment and it was the Delphi panel's view at the time of the meeting (in November 1998) that the higher published efficacy rates were not seen in clinical practice in the management of men with chronic ED. It was therefore decided that the publication by Steers *et al* (1997b) should be used as the basis of Viagra's efficacy in the economic model since the patients in this study (men with severe erectile dysfunction) were more comparable to those studied by Porst. Schwarz considered that this

explained the statement in the introduction of the article relating to Viagra '… only one study presented results in a form that allowed meaningful comparisons with other ED treatments'. The authors also stated that 'to date, most studies of sildenafil assessed efficacy using patient diaries recording individual frequencies of success' acknowledging the existence of other efficacy studies for this product. The paper by Goldstein *et al* included men with an unspecified level of ED severity and was therefore of no relevance to the pharmacoeconomic model used.

Schwarz stated that to counteract the limited efficacy data, a sensitivity analysis was conducted that varied the probability of successful treatment with Viagra from 0.25 to 0.8 in order to cover the wide spectrum of published efficacy data. The outcome of this analysis revealed that the model was robust to such changes ie the expected cost per patient started on treatment with Viagra remained below the corresponding expected cost attributable to Viridal Duo and MUSE.

Given the above, Schwarz considered that as the data for the response rates for Viridal Duo and Viagra, used in the economic model, were a comparison of like with like, the use of the study in its press release was not an inaccurate, unbalanced or unfair comparison of the two products, as alleged.

Schwarz noted that Pfizer had highlighted the incorrect referencing of one of the sildenafil studies mentioned in the introduction that reported response rates of ED, and that it was unhappy with the use of the term 'severe vasogenic aetiology' referring to a contraindication to the use of sildenafil. Schwarz considered that Pfizer needed to dispute the use of this terminology and the incorrect referencing with the authors of the article. The company noted once again that this was a peer-reviewed journal and considered that the use of this terminology did not affect the presentation of the data in the press release or the conclusion of the study.

Schwarz noted that a quote from a scientific congress was included at the end of the press release and offered some caution about the results of the study. It was stated that 'It is important to remember, however, that these are, in effect, 'virtual patients'. This is a predictive model rather than a real life situation, …'. Schwarz agreed that the results should be updated as more data became available, however, the company considered that the current conclusions were based on the most up-to-date data available at the time.

Thus Schwarz contended that the methodology and conclusions of the study were valid to date and refuted the allegation that the presentation of the study in the press release was in breach of Clause 7.2.

The press release was distributed on 5 August without copies of the references cited within it; these had to be requested separately. The press release was sent to medical and pharmaceutical publications such as Doctor, BMJ, Pulse and the Pharmaceutical Journal as well as to some freelance journalists who contributed to the lay media. The press release was also issued to Update, the newsletter of the Prostate Research Campaign, which was aimed at men with prostate problems, their wives and doctors.

PANEL RULING

The Panel noted that although the study discussed in the press release had been independently published and peer reviewed, Schwarz's use of it for promotional purposes brought it within the scope of the Code. The study (Plumb and Guest (1999)) compared the cost effectiveness of Viridal Duo relative to Viagra using an economic model based on estimates of clinical outcome and resource use obtained from published literature and a Delphi panel. The study compared the direct healthcare costs and consequences, from the perspective of the NHS, of a non-specific population of ED sufferers (unstratified by demography and aetiology). The published papers cited in support of Viagra were Steers *et al* (1997a) and Steers *et al* (1997b). It was stated that only Steers *et al* (1997a) presented results in a form that allowed meaningful comparisons with other ED treatments with response rates of 42% and 55% with the 50mg and 100mg doses respectively. This study was in men with 'broad spectrum erectile dysfunction'. The response rates of 42% and 55%, however, were in fact from Steers *et al* (1997b), a study in men with severe erectile dysfunction. (A subsequent paragraph in the paper correctly quoted the results from Steers *et al* (1997a) which had assessed efficacy using patient diaries.) The Panel noted that the Viagra SPC stated that results from clinical trials had shown that the proportion of patients reporting improvement on Viagra varied from 43% (radical prostatectomy) to 84% (psychogenic ED) according to aetiology.

The Panel noted that Goldstein *et al* (1998) had reported response rates to Viagra of up to 69% in a dose escalation study. The dose of Viagra could be increased to 100mg based on efficacy and tolerance. This study had not been cited by Plumb and Guest although it appeared to the Panel that the study population, men with erectile dysfunction of various aetiologies and of at least six months' duration, was relevant to their pharmacoeconomic model of a non-specific population of ED sufferers (unstratified by demography and aetiology).

The Panel noted that the study stated that the published literature reported response rates of between 60% (Purvis *et al* (1996)) and 80% (Linet and Neff (1994)) for Viridal Duo across all aetiologies. The study by Porst (1997) which Schwarz stated was used to establish the relative cost-effectiveness of Viridal Duo was in unselected men with chronic ED ie ED of greater than 6 months' duration. The Panel did not accept Schwarz's submission that this patient population was comparable to the population of men with severe ED studied in Steers *et al* (1997b) which the company had stated had been used as the basis of Viagra's efficacy in the economic model. In the Panel's view chronic related to the time a disease state had been present whereas severe related to the seriousness of the underlying disorder.

The Panel noted that the study by Plumb and Guest was a preliminary pharmacoeconomic model. A discussion at the end of the paper stated that there were a number of limitations to the study and the final conclusion read '… these results should be updated as more robust data become available'. The

press release ended with a consultant urologist's view of the study in which he stated 'It is important to remember, however, that these are in effect, 'virtual patients'. This is a predictive model rather than a real life situation…'. By contrast the opening paragraph of the press release stated that 'Viridal Duo is clinically more effective [than Viagra]' which, in the Panel's view, was a strong clinical claim based on preliminary economic data.

The Panel considered that the press release provided a misleading comparison of Viridal Duo and Viagra. A breach of Clause 7.2 of the Code was ruled. The Panel considered that it was inappropriate for Schwarz to distribute copies of the study for promotional purposes and a breach of Clause 7.2 of the Code was ruled.

The Panel noted that the study stated that Viagra was contraindicated for ED with severe vasogenic aetiology. This was not a contraindication listed in the Viagra SPC. By using the study Schwarz was thus providing inaccurate information about Viagra in breach of Clause 7.2 of the Code. The Panel ruled a breach of that clause.

Complaint received **26 August 1999**

Case completed **25 November 1999**

CASE AUTH/920/9/99

GENERAL PRACTITIONER v GLAXO WELLCOME

Cancelled meeting

A general practitioner complained that he had not been informed of the cancellation of a meeting due to be held by Glaxo Wellcome, even though he had returned the invitation reply slip, and he had wasted his time by travelling to the venue only to find it locked.

The Panel sent Glaxo Wellcome's response to the complainant and invited further comments and these in turn were commented upon by Glaxo Wellcome. The Panel observed that the parties' accounts differed and it was difficult in such circumstances to determine precisely what had transpired. The Panel accepted that extreme dissatisfaction was necessary on the part of an individual before he or she submitted a complaint. A judgement had to be made on the available evidence. The Panel was concerned about the inconsistencies between the parties' accounts but considered that it was not possible to determine where the truth lay. In these circumstances the Panel ruled no breach of the Code.

Upon appeal by the complainant, the Appeal Board considered that the complaint consisted of two issues; the events leading up to the cancellation of the meeting and the company's response to the complainant's letters regarding the cancellation of the meeting. With regard to the arrangements for the meeting and its subsequent cancellation, the Appeal Board noted that the parties' accounts differed and that with no documentary evidence to support either account it was impossible to determine where the truth lay. The Appeal Board upheld the Panel's ruling of no breach of the Code.

With regard to what happened after the event, the Appeal Board noted that the complainant had written to Glaxo Wellcome the day after the proposed meeting requesting an explanation as to why he had not been informed of its cancellation. The representative concerned responded quickly to the letter by visiting the complainant's surgery and although unable to see him asked his receptionist to pass on her apologies/explanation. Although the representative had responded quickly to the first letter to Glaxo Wellcome, she had failed to make personal contact with the complainant. The Appeal Board considered that in such circumstances the complainant should have been sent an explanation and apologies for the cancelled meeting in writing. The representative should not have relied upon a third party to pass on a message. Two further letters had received no written reply and although the representative once again called at the complainant's surgery no personal contact was made. The Appeal Board considered that the representative's response was inadequate and ruled a breach of the Code.

The Appeal Board noted that the two further letters were received by Glaxo Wellcome at around the time that the representative was on holiday and considered that in her absence the company should have ensured that the matter was dealt with.

COMPLAINT

A general practitioner complained that he had not been informed of the cancellation of a meeting due to be held on 30 June 1999 and organised by Glaxo Wellcome UK Limited. The complainant had wasted his time by travelling to the proposed venue only to find it locked.

The complainant stated that he had sought an answer from Glaxo Wellcome by repeated letters but had not yet heard from the company. In his letters he had expressed dissatisfaction at the company delegating responsibility to someone who turned out to be not up to it. The complainant had posted a reply slip on 3 June but no care was taken to inform him of the cancellation, made much in advance, which he discovered only when he was at the venue with yet another GP who was also as surprised.

The complainant stated that such action by a pharmaceutical company only reduced trust in it and discouraged a GP from attending future meetings sponsored by that company. The complainant stated that it was an unfortunate situation for the company not to own up to responsibility for the loss of his time.

When writing to Glaxo Wellcome, the Authority invited it to consider the requirements of Clauses 15.2 and 15.4 of the Code.

RESPONSE

Glaxo Wellcome stated that the meeting entitled 'Is it another headache?' was organized by representative A in early May. Invitations were sent out at the end of May, and GPs were asked to send reply slips to representative B as representative A was due to start a new job. Representative B did not receive a reply slip from the complainant.

One week before the meeting was due to take place, only 12 GPs had agreed to attend. On 24 and 25 June representative B and fellow representative C called all surgeries in the area to find out if anyone else planned to come along, but had not yet replied to the invitation. No other delegates were recruited. At this point it was decided to move the meeting to a smaller venue and they notified the original venue of their decision to cancel.

On Monday, 28 June, representatives B and C contacted all 12 GPs to notify them of the change of venue. Ten GPs said they wouldn't be able to come after all. Thus, with just two GPs left, it was decided to cancel the meeting completely.

Glaxo Wellcome stated that the complainant sent a letter to customer services on 5 July and representatives B and C were notified of this immediately. They explained that they had not received a reply slip from the complainant and, therefore, had no idea that he planned to attend the meeting. The representatives were asked if they could contact him to explain why the meeting had been cancelled.

During the week commencing 5 July, representative B called at the complainant's surgery and spoke to his daughter/receptionist and explained who she was and why she would like to speak to him. She was not allowed into the surgery. The complainant's daughter then came out and told her that he was too busy to see her and, rather than come back later, she should tell her anything he needed to know and she would pass it on. Representative B explained why the meeting had been cancelled and that she had no idea that the complainant had planned to attend, as he had not returned his reply slip. His daughter then told her that she had sent the slip herself and that there was no reason why it should not have been received. Once again the representative apologized for any inconvenience caused to the complainant and repeated that she had not received his reply. She gave the receptionist/daughter her business card and told her that if the complainant required any further information, she would be happy to speak to him.

During the week commencing 16 August, the complainant contacted customer services to complain that he had not been contacted by the company regarding his initial complaint.

Representative B explained to customer services that the complainant had refused to see her. The following week she called again at the complainant's surgery in the early afternoon. There appeared to be someone inside, however the intercom was not answered. Since then she had made no further attempt to contact him.

Glaxo Wellcome stated that representative B was experienced and often organised educational meetings in the area and had had no previous problems or complaints regarding any meetings she had been involved in over the last seven years. She had passed the ABPI examination in May 1993.

From the above, Glaxo Wellcome felt comfortable that the representatives, at all times, maintained a high standard of conduct, both in contacting doctors who returned the reply slips to notify them of the cancellation, and in dealing with the complainant's complaint to customer services, making every endeavour to see him to explain the situation and apologize for any perceived inconvenience caused. Glaxo Wellcome thus considered that the representative involved had not been in breach of Clauses 15.2 and 15.4 of the Code.

In response to a request from the Panel for clarification of certain points, Glaxo Wellcome confirmed that representative B did compile a list of GPs to be invited to the meeting. The complainant was included on this list and was therefore invited to the meeting. Representative B also kept a list of GPs who had replied to the invitation indicating their intention to attend. The complainant was not on this second list as a reply slip was not received from him.

All GPs who did not reply to the invitation (including the complainant) were telephoned by either representative B or C one week before the meeting was due to take place. In situations where they could not speak to the GP directly, a message was left with either practice staff or on an answerphone. GPs planning to attend the meeting were asked to telephone representative B or C as soon as possible.

FURTHER COMMENTS FROM THE COMPLAINANT

The response from Glaxo Wellcome was passed to the complainant for further comment. The complainant stated that Glaxo Wellcome was wrong to state that GPs were asked to send reply slips to representative B. In fact the reply slips indicated that they were to be sent to person D. The complainant confirmed that he had posted the reply slip to person D on 3 June and also left a message on her answering machine for her to ring him which she did on 18 June. During this telephone conversation the complainant informed person D that he had posted to her the reply slip for the meeting. The complainant stated that at that point, person D did not talk about any proposed or decided cancellation of the meeting rather she encouraged him to attend future such meetings even if he had not sent in a reply slip. The complainant stated that at no time before 30 June did anyone contact him regarding the cancellation of the meeting.

The complainant stated that representative B came suddenly to his surgery completely unannounced and wanted to see him about the above meeting, his receptionist informed her that he was rather busy but asked her to send in a written reply if she wished and say whatever she had to. No such reply was ever received.

The complainant was surprised that Glaxo Wellcome did not refer to person D in its response but instead referred to representative B who was completely unknown to him before she gave him her business card when she called as described above.

The complainant queried why Glaxo Wellcome should apologize to him if it refused to accept that he did apply to person D.

The complainant stated that Glaxo Wellcome should own up to its responsibility for the breakdown of communication and come clean as to why this actually happened.

FURTHER COMMENTS FROM GLAXO WELLCOME

The complainant's comments were passed to Glaxo Wellcome. Glaxo Wellcome explained that person D was not an employee of the company. She was formerly the postgraduate secretary at the local district general hospital but had since retired from this position, but continued to work with the chairman of the postgraduate centre. She had much experience of organizing mailings and invitations for speaker meetings, and continued to do this for many different pharmaceutical companies.

Glaxo Wellcome stated that, at the choice of the representative, reply slips could be returned to either the representative or to person D. In this case, representative B specifically asked for the reply slips to be returned to her home address in an attempt to reduce the level of communication necessary between herself and person D. Representative B's Freepost address was printed on the reply slip. Therefore, on this occasion, person D's role was purely to act in an administrative capacity, mailing the invitation letter out to all GPs in the area, including the complainant.

Glaxo Wellcome noted that the complainant made reference to having sent a reply paid slip to person D and then having contacted her on the telephone. Person D had absolutely no recollection of having any communication, other than sending the invitation, with the complainant regarding this meeting. In her recollection no telephone conversation was held with the complainant and no message was left on her answering machine. She did wonder whether the complainant could possibly be confusing this meeting with one held by another pharmaceutical company around a similar time.

In response to a request from the Panel for documentation from the meeting, Glaxo Wellcome confirmed that it was unable to supply a copy of the reply slip used. Representatives B and C had disposed of the slips after contacting the doctors who had replied to the invitation following the cancellation of the meeting and person D did not have either an electronic or actual copy of the invitation and reply slip.

PANEL RULING

The Panel observed that the parties' accounts differed and that there was no documentary evidence to support either account. It was difficult in such circumstances to determine precisely what had transpired.

The Panel accepted that extreme dissatisfaction was necessary on the part of an individual before he or she submitted a complaint. A judgement had to be made on the available evidence. The Panel was concerned about the inconsistencies between the parties' accounts but considered that it was not possible to determine where the truth lay. In these circumstances the Panel decided to rule no breach of Clauses 15.2 and 15.4 of the Code.

APPEAL BY COMPLAINANT

The complainant stated that the grounds for his appeal against the Panel's decision were:

1 Glaxo Wellcome was asked to, but had failed to, prove that in fact he, as a GP, was invited to the said 30 June meeting by returning a tear-off slip to be sent to representative B and not to person D. The company had retained no tear-off slips from GPs in spite of his quick complaint sent to it just one day after the meeting on 1 July. A copy of the complainant's letter was provided.

2 Glaxo Wellcome could not deny that the complainant was on the list of the invited GPs but had failed to prove that he was not on the list of GPs who had replied to the invitation wishing to attend the 30 June meeting.

3 Glaxo Wellcome had actually admitted entrusting/employing person D to receive tear-off slips sometimes. There was also some evidence to this effect (a) there was no tear-off slip attached to the leaflet of invitation to the meeting as it had been posted to person D, (b) the other 13 July meeting leaflet also faxed with (a) and the complainant's letter of 6 November showed the method of invitation at the time – by pharmaceutical companies. In fact person D had actually admitted speaking to the complainant when she was contacted by Glaxo Wellcome as per its letter of 6 October and due to whatever reason chose to forget, the complainant stated that even without talking to him she opined that he was possibly confusing the Glaxo Wellcome meeting with one to be held by another pharmaceutical company around a similar time. If one believed Glaxo Wellcome, person D had nothing to do with the meeting. Why was it that she was entrusted by Glaxo Wellcome to send the invitation to the complainant for this 30 June meeting?

RESPONSE FROM GLAXO WELLCOME

Glaxo Wellcome stated that its position in this case had not changed. As previously stated Glaxo Wellcome naturally regretted any inconvenience experienced by the complainant, but it did not feel responsible for that inconvenience.

Glaxo Wellcome's previous submissions contained full details of the case from the Glaxo Wellcome perspective but it would briefly discuss the points it would like to cover at the appeal which were:

1 The timetable of events

The complaint concerned a meeting entitled 'Is it Another Headache?'. This meeting had been

organised by Glaxo Wellcome's representative A who was about to leave to take up a position at head office. The complainant had submitted his copy of the programme to the Authority. Although Glaxo Wellcome did not have an original of the actual invitation to the meeting in question, it would show a copy of an invitation to another meeting, with the response slip at the foot of the letter.

a) Role of person D

The invitations were sent out by person D, who had been employed previously as the postgraduate secretary at the local district general hospital, but who still did post-retirement work with the doctor who was chairing this meeting. At representative B's request, person D had asked for the reply slips to be sent directly to the Freepost address of representative B, and not to her.

b) Role of representative B

Representative B was responsible for collating the responses from doctors who wished to attend the meeting and checking their names against the invitation list. After calling all the surgeries in the area to see whether any one else was going to attend (24/25 June), it became apparent that only twelve doctors would be attending. It was therefore decided to change the venue to one that was smaller. When those who had originally planned to attend were informed of the change (28 June), only two doctors were still able to come and the decision was made to cancel the meeting.

The two remaining doctors were informed. As no one else had expressed their intention to attend there was no need to inform anyone else of the cancellation of the meeting.

c) The complainant

The complainant had been invited to the meeting. No reply was received by representative B at her Freepost address. In the absence of a reply, the complainant was telephoned on 24/25 June and if it was not possible to speak with him directly, a message would have been left for him, asking whether he planned to attend the meeting at the original venue.

2 Events following the receipt of a complaint from the complainant

A letter from the complainant was received on 5 July in Glaxo Wellcome's customer services department. It was immediately passed to representative B for her to respond personally. During the week beginning 5 July, representative B called at the complainant's surgery, access to which was restricted and required communication through a speaker. She spoke to the complainant's daughter/receptionist and explained who she was and the purpose of her visit. She was not allowed to enter, but the complainant's daughter came out to her and explained that the complainant was too busy to see her but had asked her to tell his daughter all he needed to know and she would pass it on to him.

Representative B explained why the meeting had been cancelled and that as she had not heard from the complainant she was not expecting him to attend. His daughter said that she had returned the slip herself and could not understand why it had not been received. After apologising for any inconvenience that the complainant had experienced, representative B gave her business card to the complainant's daughter and said that she would be happy to speak to the complainant if he required further information. No mention was made of the need to provide a written reply to the complainant.

A further letter from the complainant, written on 28 July, was received on 29 July but there was no record of any letter of 10 July having been received. On this occasion the complainant expressed dissatisfaction with the response that he received and suggested that he should receive compensation for his lost time. Following a further letter, received by customer services on 16 August (sent by fax on Saturday, 14 August), representative B visited the surgery again, during the following week. Although there appeared to be someone inside the surgery there was no reply to the intercom. This was her last attempt to see the complainant.

The complainant had consistently stated that he returned his reply slip to person D. When Glaxo Wellcome spoke to her on 6 October, she had no recollection of having had any communication either with or from the complainant regarding this meeting. She had had no telephone conversation with him and said that no message had been left on her answering machine. She had wondered whether the complainant had confused this meeting with one held by another pharmaceutical company at about that time.

Neither person D nor representative B had kept a copy of the original invitation and reply slips. The reply slips had been destroyed after the meeting was cancelled and no master copy had been retained by person D, who had sent out the invitations.

Representative B was a representative of seven years' standing. She regularly organized meetings and had had no problems with any meetings that she had organized in the past.

Glaxo Wellcome submitted that representative B, with appropriate support from her colleagues, had behaved professionally and responsibly throughout. She went to some lengths to assure that all doctors who had responded positively to the meeting invitation were informed of developments as they occurred, especially when the meeting was cancelled. She responded promptly to deal with the complaint, but unfortunately this did not meet with the complainant's approval. She apologised on behalf of the company as Glaxo Wellcome did not wish to see any of its customer's dissatisfied and holding any grievance, whatever the cause.

Glaxo Wellcome did not believe that the representative was at any time in breach of either Clause 15.2 or 15.4.

FURTHER COMMENTS FROM THE COMPLAINANT

The complainant stated that Glaxo Wellcome stated that its position in this case had not changed. But it had changed and he would explain how below.

Referring to the paragraph 'Role of person D'. At the representative's request person D had asked for the reply slip to be sent directly to representative B's Freepost address and not to her (D) – this was a white lie at least in the case of the leaflet sent to the complainant. There was no mention of representative B's name at all or else the complainant would have sent the reply slip to representative B and said so.

It appeared that Glaxo Wellcome thinks and says it has actually destroyed all the evidence so soon to sound very simply and make believe whatever it says – but it failed the company rather than the complainant who had provided as much evidence as could possibly be produced. If lies were repeated several times – those who spoke and maybe some of those who heard it would start believing it as a truthful statement. Glaxo Wellcome's attempt to make the complainant a liar should be frustrated. That was exactly what Glaxo Wellcome was trying to prove.

Now Glaxo Wellcome was changing its story when it mentioned that the complainant was telephoned on 24/25 June asking through a message left whether he planned to attend the meeting at the original venue. This was a very new concoction never heard before in Glaxo Wellcome's letters as the complainant had thoroughly asked all those supposed to take messages on his behalf and no one ever had any such message.

Glaxo Wellcome mishandled all these, destroyed evidence and now wanted to get away clean. The complainant hoped this did not happen.

APPEAL BOARD RULING

The Appeal Board considered that the complaint consisted of two issues; the events leading up to the cancellation of the meeting and the company's response to the complainant's letters regarding the cancellation of the meeting.

With regard to the arrangements for the meeting and its subsequent cancellation, the Appeal Board noted that the parties' accounts differed and that with no documentary evidence to support either account it was impossible to determine where the truth lay. In these circumstances the Appeal Board upheld the Panel's ruling of no breach of Clauses 15.2 and 15.4 of the Code.

With regard to what happened after the event, the Appeal Board noted that the complainant had written to Glaxo Wellcome the day after the proposed meeting requesting an explanation as to why he had not been informed of its cancellation. Representative B responded quickly to the letter by visiting the complainant and although unable to see him asked his receptionist to pass on her apologies/explanation. Two further letters were sent by the complainant to Glaxo Wellcome, on July 28 and August 16; following the second of these letters, and having just returned from holiday, representative B again called at the complainant's surgery but was unable to make contact. Since then the representative had not tried to contact the complainant.

The Appeal Board noted that although the representative had responded quickly to the first letter of complaint (dated 1 July) she had failed to make personal contact with the complainant. The Appeal Board considered that in such circumstances the complainant should have been sent an explanation and apologies for the cancelled meeting in writing. The representative should not have relied upon a third party to pass on a message. Two further letters (dated 28 July and 16 August) received no written reply and no personal contact was made. The Appeal Board considered that the representative's response was inadequate and ruled a breach of Clause 15.2 of the Code.

The Appeal Board noted that the two further letters were received by Glaxo Wellcome at around the time that representative B was on holiday and considered that in her absence the company should have ensured that the matter was dealt with.

The appeal was thus partially successful.

Complaint received **6 September 1999**

Case completed **24 December 1999**

CASE AUTH/921/9/99

LUNDBECK v LILLY

Promotion of Prozac

Lundbeck complained about a promotional campaign for Prozac (fluoxetine) undertaken by Lilly. In particular Lundbeck was concerned about a 'Dear Doctor' letter headed 'PROZAC – How to achieve NHS Cost Savings' which stated that the expiry of the Prozac patent in January 2000 was expected to lead to a fall in the Drug Tariff price of fluoxetine. Lundbeck alleged that the claim that substantial cost savings could then be made by switching patients to fluoxetine was incorrect. It was untenable to believe that all patients currently on other antidepressants could be switched to fluoxetine merely in the interests of hypothetical cost savings. Lundbeck further alleged that in a letter sent to pharmacists the price of Cipramil (Lundbeck's product citalopram) was wrong. Lilly had not indicated that it would withdraw the materials and Lundbeck alleged that it was bringing the industry into disrepute.

The Panel noted that the campaign was based on conjecture of what might happen to the price of fluoxetine once the Prozac patent expired. A price comparison model for fluoxetine and the other SSRIs had been based on what had happened in 1997 to the price of captopril and the other ACE inhibitors once the captopril patent had expired. The Panel queried the validity of this. In the Panel's view, it was misleading to base the cost comparison on estimated savings. There was no way of substantiating the material until after Prozac had come off patent and the cost each month was known. The Panel ruled breaches of the Code. A breach of the Code was also ruled because the price of Cipramil had been given wrongly in a letter to pharmacists. Lilly had become aware of the price reduction two days before the mailing had been sent out. The Panel did not think that the campaign discredited the industry and no breach was ruled in that regard.

Upon appeal by Lilly of the ruling relating to the post-patent expiry cost comparison, the Appeal Board noted that the cost comparison chart detailed the month by month cost of Prozac/fluoxetine and its competitors to the nearest penny. Various sections were labelled 'Estimated savings' although the title of the chart made no reference to the fact that the costs contained therein were estimated. In the Appeal Board's view it was not obvious that the costs stated were an estimate of what might or might not happen to prices following patent expiry. Regardless of the labelling of the price comparison chart, or the suitability of the model upon which it was based, the Appeal Board considered it was misleading to base the cost comparison on estimated savings and what might happen. The cost comparison was not accurate. There was no way of substantiating the material until after Prozac had come off patent and the cost each month was known. The cost of the competitor products might also change. The Appeal Board upheld the Panel's ruling of breaches of the Code.

Lundbeck Ltd complained about a promotional campaign for Prozac (fluoxetine) undertaken by Eli Lilly and Company Limited. In particular the company was concerned about a 'Dear Doctor' letter headed 'PROZAC – How to achieve NHS Cost Savings'. The letter stated that the expiry of the patent on Prozac in January 2000 was expected to lead to a fall in the Drug Tariff price of fluoxetine for the treatment of depression.

It was noted in the letter that in other cases of patent expiry prescribing costs had not fallen, as would be expected from generic competition, but had increased due to the continued use of newer treatments which offered a clinical benefit over the medicine which had lost its patent. The letter stated that in the case of Prozac, however, no such new medicines had been introduced. Readers were informed that by supporting the use of Prozac/fluoxetine they would be helping the NHS save money. Lilly stated in the letter that after patent expiry it would continue to promote the Prozac brand and associated services. There then followed five bullet points regarding the use of Prozac. The final bullet point stated that the Drug Tariff price for treating depression with a six month course of Prozac/fluoxetine was likely to be less expensive than any other branded selective serotonin reuptake inhibitor (SSRI) as early as November 1999. Readers were referred to a table on page 2 of the letter.

The table showed the cost of fluoxetine 20mg as £20.77 from October 1999 through until February 2000. There were expected to be successive decreases in price over the next four months until June 2000 when it stabilised at £9.72. The cost of three other SSRIs, (citalopram 20mg, paroxetine 20mg and sertraline 50mg), was expected to stay constant. If a six month course of fluoxetine was initiated in November 1999 its total cost would be £1.63 less than a six month course of citalopram started at the same time. Post-patent, and following the expected significant fall in the cost of fluoxetine, a six month course initiated in March 2000 would cost £45.48 less than a similar course of citalopram started at the same time. A footnote to the table stated that the cost comparison model was based on the patent expiry of captopril.

COMPLAINT

Lundbeck stated that it had twice contacted Lilly regarding concerns that it had relating to the letter, but had not received any response from the company.

Lundbeck stated that its concerns related to price claims versus its product Cipramil (citalopram) and other antidepressants. Lilly had claimed that post-patent expiry, substantial cost savings could be made by switching patients to generic fluoxetine. Lundbeck alleged that the claims made were incorrect and were being made when Lilly knew them to be false. The price of Cipramil given in a second letter sent to a pharmacist on 1 September, and entitled 'Eli Lilly and Company will continue to support Prozac …', was

again wrong and despite Lundbeck's earlier letter to Lilly, Lilly had not made any effort to correct this error.

Lundbeck noted that the 'Dear Doctor' letter stated that 'The past is not always a good predictor of the future'. This was followed by a sweeping statement that 'no new drugs have been introduced which are generally accepted to offer a clear therapeutic advantage'. These statements made the letter unreliable as a basis upon which to base any sort of therapeutic decision. It was simply untenable to believe that all patients currently on other antidepressants could be switched to fluoxetine merely in the interests of hypothetical cost savings.

Lundbeck had pointed out to Lilly that distribution of materials known to contain errors was a clear breach of the Code but had received no indication that the company would withdraw the incorrect materials. In distributing information known to be erroneous, Lilly was bringing the pharmaceutical industry into disrepute, in breach of Clause 2 of the Code as well as Clauses 7.2 and 7.3.

Following a request from the Panel for clarification, Lundbeck confirmed that in July 1999 the cost of Cipramil 20mg x 28 had been £16.79 (£17.99 for a 30 day supply). This price had been effective since October 1998. On 2 August 1999 the price of Cipramil 20mg x 28 was reduced to £16.19. This price change had been communicated in a letter to all wholesalers and to all relevant medical journals and price information was included in the company's advertisements in GP and hospital weekly and monthly journals. This information was also included in an article in Prescribers' Journal on 6 August. On 1 October the cost of Cipramil 20mg x 28 was further reduced to £16.03. This information was communicated in a letter to all wholesalers and a press release to medical journals. Details of the price were also included in the company's advertisements in GP and hospital journals. The price change was also communicated in the MIMS entry for October and also in a Prescribers' Journal entry.

RESPONSE

Lilly addressed each of Lundbeck's concerns.

1 Incorrect claims being made when the company knew them to be incorrect

Lilly stated that it sought to offer an estimate of possible cost savings to be made by prescribers following Prozac's patent loss. The company based its post-patent price estimates on the pattern of price changes seen with the ACE inhibitor captopril following its patent loss. This model was chosen as Lilly considered that it closely mirrored the Prozac situation (The presence of a number of similar products in the market place, and no paradigm shift in available treatments around the time of patent expiry). The use of the captopril model to estimate possible price changes post-patent expiry was clearly stated below the cost comparison table, and no guarantees were offered that patent loss would result in the prices shown. Lilly submitted that on the basis of the captopril model, the estimated price changes for Prozac were fair and reasonable, and the basis for these estimations was clear.

Lilly noted that Lundbeck itself had highlighted the phrase 'The past is not always a good predictor of the future' in its complaint. Lilly suggested that its use of this phrase was in fact further evidence of the company's desire to make it clear that the prices quoted were estimations based on a historical model, and that however sound its reasons for believing that it offered a fair estimation, there was no guarantee that they would turn out to be correct. Furthermore, although Lundbeck chose to dispute the specifics of Lilly's estimates, there could surely be no doubt that the price of fluoxetine would fall dramatically post-patent expiry.

Lilly stated that with respect to Lundbeck's allegation that its claims were made when it knew them to be incorrect was plainly absurd as the company had taken the best historical example of a product going off patent.

2 Failure to respond to Lundbeck's letters

Lilly stated that Lundbeck's initial letter outlining its concerns was dated 13 August and received a few days later. Due to a number of key members of staff being on holiday, a response was still being finalised when Lundbeck's second letter was sent. The second letter, dated 3 September, threatened referral of the complaints to the Authority if a satisfactory response had not been obtained by 2pm on 6 September but was not received by Lilly's medical director until the afternoon of 6 September, by which time it appeared that Lundbeck had already made its complaint to the Authority. Lundbeck stated that it attempted to telephone the medical director at Lundbeck the next morning to discuss the matter with him, but he was out of the office and was not expected back until Friday, 10 September.

Lilly stated that whilst it regretted the delay in responding to Lundbeck's initial letter, the follow-up letter was received by its medical director after the deadline contained within it. The earliest that the letter could have been received was in the morning of the same day, and even then it would have been very difficult to arrange an appropriate response to what was effectively a new complaint at such short notice. This behaviour was of serious concern to Lilly. Lilly stated that Lundbeck had sought to strengthen its argument by highlighting a supposed repeated lack of response to its communications. It was clear that it was never Lundbeck's intent to resolve this matter without recourse to the Authority, and that the second letter was sent purely to discredit Lilly in the eyes of the Authority.

3 Distribution of promotional material containing wrong price for Cipramil

At the time of mailing, the promotional material referred to within Lundbeck's initial complaint showed the correct price for Cipramil. A follow-up mailing was then prepared, and final authorisation was given for its distribution on 20 August 1999. Lundbeck subsequently reduced the price of

Cipramil. As far as Lundbeck was aware, the first occasion that Cipramil's new price appeared in print in the public domain was in 'Chemist & Druggist', 21 August, and the first time that it saw it was on Monday, 23 August.

Lilly stated that although it could sympathise with Lundbeck's frustration that materials containing an incorrect price for Cipramil were in circulation, with the best will in the world, if a one-off mailing was sent out, and a price was subsequently changed, there was little the company could do about letters that had already been sent, other than to distribute updated versions of the materials which it did in fact do. Lilly stated that it had taken steps to ensure that further materials stating an erroneous price for Cipramil would not be sent out or used by medical representatives for detailing customers now that the price had changed.

4 Use of cost-savings as an inducement to prescribe

Lilly noted that Lundbeck stated that 'It was simply untenable to believe that all patients currently on other anti-depressants could be switched to fluoxetine merely in the interests of hypothetical cost savings'. Lilly stated that at no time did it suggest that a hypothetical cost saving should be by any means the only factor involved in a decision about possibly switching patients from one antidepressant to another. This having been said, however, price was obviously a factor in prescribing. Lundbeck itself appeared to believe this also, having recently cut the price of Cipramil on two occasions such that it maintained its position as the lowest priced branded SSRI, whereas the price of Prozac had remained the same during this period.

Lilly provided copies of a number of items used in the campaign at issue. The 'Dear Doctor' letter headed 'PROZAC – How to achieve NHS Cost Savings' had been sent to the mailing house on 20 July 1999 and posted on 22 July. The cost of a six month course of citalopram was given as £107.94. This letter was not used after 4 September. A subsequent letter entitled 'Eli Lilly and Company Limited will continue to support Prozac…' was sent to the mailing house on 20 August and posted on 25 August. The cost of a six month course of citalopram was again given as £107.94. This second letter also contained a graph which showed that immediately post-patent expiry the patent price of captopril was maintained but between 2 and 3 months post-patent the price almost halved and continued to fall slowly until 8 months post-patent when the price was just less than half that which it had originally been. There was also a bar chart showing how ACE inhibitor sales had increased in the years since the patent had expired on captopril.

Two advertisements which had appeared in the Pharmaceutical Journal were also provided. Both had been prepared in August 1999 but one (ref PZ1171, published 21 August) stated that based on the expected price reduction of fluoxetine, a six month course of treatment post-patent expiry could yield expected savings of up to £41.70 over the least expensive branded SSRI currently on the market. The other advertisement (ref PZ1196, published 4 September) only referred to an expected saving of over £40.

Following a request for further information Lilly confirmed the dates that the 'Dear Doctor' letter and the subsequent letter had been approved for use and mailed. Although 5,301 of the letter entitled 'Eli Lilly and Company Limited will continue to support Prozac …' were sent out by the mailing house on 25 August 1999 a further 19 copies were sent on 1 September. Lilly conceded that the sending of these further copies containing the wrong price for Cipramil was authorised after the new price had appeared in print and apologised for this. The company refuted the allegation that this had been done knowingly; the staff member responsible for the campaign was on leave at the time, only returning on 6 September at which time the letter was updated with the new price of Cipramil.

Lilly stated that the lead time to stop a mailing was, in theory, the time it would take to telephone the mailing house to request that the mailing be stopped. In the case of the letter mailed in August and on 1 September the member of staff responsible was on leave and so the mailing was not stopped until his return.

PANEL RULING

The Panel noted that the 'Dear Doctor' letter which was approved for use on 20 July 1999 and mailed on 22 July gave the cost of Cipramil 20mg x 30 as £17.99. This was the correct price for the product at that time. A subsequent letter was approved for use on 20 August and mailed on 25 August and also gave the cost of a 30 day supply of Cipramil as £17.99. The cost of Cipramil 20mg had, however, been reduced on 2 August such that a 30 day supply now only cost £17.35. The Panel noted Lundbeck's submission that it had communicated the price decrease via the medical press. In that regard the Panel noted that the August 1999 MIMS carried the old price ie £16.79 for a 28 day pack as did advertisements appearing in Hospital Doctor (5 August) and Pulse (August 7). Subsequent issues of Pulse (14 August and 21 August) did not carry an advertisement for Cipramil and nor did any copy of GP for the first three weeks of August. Hospital Doctor (19 August) carried the new price for Cipramil. Although the Prescribers' Journal (6 August) informed readers of the price reduction the Panel noted that this publication had a circulation of only 1,500 (ref Willings Press Guide 1998) and in its view the new price of Cipramil did not appear generally until mid August 1999. The Panel noted that Lilly had become aware of the price decrease on 23 August via the Chemist and Druggist – two days before the second letter, now with the wrong price of Cipramil, was due to be mailed. The lead time to stop a mailing was the time taken to telephone the mailing house but the mailing was not stopped until 6 September when the person responsible for the campaign returned from holiday. The Panel considered that this was unacceptable, during holiday periods companies must ensure that someone else took responsibility. The second letter thus gave inaccurate information about Cipramil. A breach of

Clause 7.2 was ruled. This ruling was accepted by Lilly.

The Panel noted that the campaign was based on conjecture of what might happen to the price of fluoxetine once the Prozac patent expired in January 2000. A price comparison model for fluoxetine and the other SSRIs had been based on what had happened in 1997 to the price of captopril and the other ACE inhibitors once the captopril patent had expired. The Panel queried the validity of this given the difference in therapy area and the fact that since the introduction of twice daily captopril other ACE inhibitors had only required once daily dosing which, in the Panel's view, would offer a therapeutic advantage in the management of hypertension. The Panel queried whether the data was accurately based on the captopril model as the Drug Tariff price for captopril had remained constant in March and April following patent expiry in early February. The May Drug Tariff recorded a much reduced price for captopril. The cost comparison model for the SSRIs, however, showed that following patent expiry in early January the cost of fluoxetine would only remain constant in February with a sharp fall in price occurring in March. The Panel did not accept that the Prozac material had followed the captopril example as if it had the price of fluoxetine would not have dropped until April 2000. A further confounding factor was that the price of Cipramil had changed twice since the chart was produced. Notwithstanding the Panel's query regarding the validity of the model, the Panel noted that Clause 7.2 of the Code required that information claims and comparisons must be, *inter alia*, accurate; Clause 7.3 also required that they be capable of substantiation. In the Panel's view, it was misleading to base the cost comparison on estimated savings. There was no way of substantiating the material until after Prozac had come off patent and the cost each month was known. The Panel ruled breaches of Clauses 7.2 and 7.3 of the Code.

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

The Panel noted that Lundbeck had written to Lilly on 3 August with its concerns about the 'Dear Doctor' letter. Three working weeks later a reply had not been received. The Panel noted that staff holidays had contributed to this delay but considered it unfortunate that Lilly had not even acknowledged Lundbeck's letter. Although it was encouraged by the ABPI, there was, however, no obligation within the Code for companies to respond to criticism of their promotional practices except when such criticism was directed through the Authority. The matter was not subject to the Code and the Panel made no ruling in this regard.

APPEAL BY LILLY

Lilly accepted the Panel ruling that the 'Dear Doctor' letter mailed on 25 August contained inaccurate information about the Cipramil price. This had been corrected and it had implemented processes to ensure that this did not occur again.

Lilly also accepted that the letters using the captopril model showed reductions in the estimated post-patent fluoxetine price one month earlier than corresponding falls in the price of generic captopril. This oversight was however remedied in subsequent promotional materials. Lilly regretted the circumstances which led to inaccurate information on citalopram appearing and had taken steps to prevent this occurring again.

Lilly appealed the ruling that it was in breach of Clauses 7.2 and 7.3 of the Code in relation to the conjecture concerning what might happen to the price of fluoxetine when the patent on Prozac expired in January 2000.

Lilly stated that the Panel had found Lilly in breach of Clause 7.2 because it considered that the cost comparison was misleading as it was based on estimated savings. Lilly believed that it was not misleading to base a cost comparison on estimated savings provided that this was made clear. Lilly believed that the crux of this matter lay with whether the healthcare professionals reading the materials would have been in any doubt that the quoted figures were estimates based on an historical model. Lilly believed that its materials made it clear that it was using a previous patent expiry model by way of example in order to estimate what the possible savings in respect of fluoxetine could be. It was also made clear that the model was 'an example' and that the savings were only 'estimates'. Lilly noted that it also stated that 'The past is not always a good predictor of the future' which again made the point that the prices quoted were based on an historical model and that there were no guarantees that these prices would be realised. If Lilly had sought to convince the reader that the quoted figures were actually accurate predictions and that the estimated savings were guaranteed, then Lilly would accept that this was misleading. That was, however, simply not the case. Also, the materials consisted of letters, the front page of which detailed the message, with the back page providing the supporting evidence. The message on the front page was that fluoxetine was 'likely to be less expensive', 'reduce your costs' etc. It did not specify an actual amount. Bearing in mind that Prozac was going off patent, surely there could not be any argument that fluoxetine would be less expensive and hence reduce costs. The second page substantiated further these statements by giving the most, in Lilly's view, appropriate example of a product that had gone off patent to show what could happen and quantifying what the savings might be. The second page made it clear that Lilly had used the captopril historic model and that the savings were an estimate. It was not until the healthcare professional got to the second page that they saw the model and the estimates. The key message was that use of fluoxetine could save prescribers money after patent loss.

Bearing in mind the wording used, it was hard to see how a healthcare professional could see this as anything other than what it was – an estimate of what might or might not happen in the future and nothing more. Lilly strongly believed that it had presented a clear and unambiguous message in the materials concerned. Lilly had stressed that the quoted figures

were estimates, and had made it clear how these figures had been derived. Lilly therefore failed to see how the promotional materials concerned could possibly be considered misleading, and was at a loss to understand how its use of the cost comparison model could be ruled to be in breach of Clause 7.2.

In relation to Clause 7.3 Lilly noted that this clause stated that 'Any information, claim or comparison must be capable of substantiation.'

The price of fluoxetine would fall post-patent expiry, and Lilly had sought to offer an estimate of possible savings on the basis of the captopril model. It was obviously not possible at this point to substantiate what the cost savings would be until after patent expiry, but as Lilly was merely offering estimates rather than claiming definitive savings, it did not believe it was necessary to substantiate them beyond making it clear upon what its estimates were based, and furthermore making it clear that its figures were estimates which it had done. Lilly also needed to substantiate the prices that it was using with respect to the products that were being compared, and noted that there had been no complaint in this respect (save for the inaccuracy on the Cipramil price which had now been corrected).

Lilly believed that the comparison provided could quite reasonably be substantiated by application of the captopril model. The basis of Lilly's use of the captopril model to predict possible fluoxetine price changes post-patent loss was stated in its initial response. In summary, Lilly considered that the presence of a number of similar products in the market place and the lack of a paradigm shift in available treatments around the time of patent expiry closely mirrored the Prozac scenario. The Panel had queried the validity of the captopril example due to the introduction of once daily dosing which it considered would offer therapeutic advantage. Once daily dosing, in Lilly's view, offered a degree of therapeutic advantage, but certainly did not constitute a paradigm shift in available treatment (like the move from tricyclic antidepressants to SSRIs). Lilly acknowledged that the captopril model might not be a perfect model of what would happen to fluoxetine post-patent expiry, but considered it provided by far the closest fit.

Lilly stated that it took a fair and balanced approach when considering the campaign and post-patent price change scenarios which might have allowed it to estimate greater fluoxetine savings were dismissed as not being sufficiently similar to the Prozac scenario.

Lilly stated that it was not misleading to base a cost comparison on estimated savings provided that this was made clear. Lilly believed that its materials made it clear that it was using a previous patent expiry model by way of example in order to estimate what the possible savings in respect of fluoxetine could be. It was also made clear that the model was 'an example' and that the savings were only 'estimates'. Lilly noted that it had also stated 'The past is not always a good predictor of the future' which again made the point that the prices quoted were based on an historical model and that there was no guarantee that these prices would be realised. Absolutely no guarantees were given that the estimates reflected anything other than a figure based upon historical precedent. Bearing in mind the wording used, it was hard to see how a healthcare professional could see this as anything other than what it was, ie an estimate of what might or might not happen in the future and nothing more. Lilly maintained that the captopril model did provide a reasonable basis for comparison, and that its use of this model and its subsequent estimates of possible price changes and promotional materials were based on an up-to-date evaluation of all the relevant and available evidence.

The individuals who were sent the promotional materials in question were educated healthcare professionals. Lilly believed that such individuals were quite capable of forming their own opinion regarding the information being presented provided that they were given sufficient background on how the information had been arrived at. They were at liberty to dismiss Lilly's use of the captopril model if they considered that the model did not apply. What was important was that Lilly had clearly explained its reasoning and the basis for its suggestions. Lilly had misled no-one, and was happy for healthcare professionals to weigh the evidence and come to their own conclusions.

A further point was the fact that the materials were sent only to healthcare professionals with a responsibility for formulary and budget planning. Lilly believed that many of its customers valued this type of information about possible future cost implications in order to assist them in their financial planning, and felt that a negative ruling on the use of predictive data set a bad precedent if Lilly was to provide its customers with the information they needed to help them do their jobs. Its feedback so far from customers had been generally favourable.

Lilly freely acknowledged that the promotional campaign was unusual. However, it honestly believed that when the facts relating to this campaign were carefully examined no breaches of the Code would be found to have occurred.

APPEAL BOARD RULING

The Appeal Board noted that the cost comparison chart detailed the month by month cost of Prozac/ fluoxetine and its competitors to the nearest penny. The Appeal Board noted that various sections were labelled 'Estimated savings' although the title of the chart made no reference to the fact that the costs contained therein were estimated. In the Appeal Board's view, and contrary to the submission by Lilly, it was not obvious that the costs stated were an estimate of what might or might not happen to prices following the expiry of the Prozac patent.

The Appeal Board did not consider that it had been shown that the captopril model was wholly applicable to Prozac and the rest of the antidepressant market.

The Appeal Board noted that Clause 7.2 stated, *inter alia*, that claims must be accurate and Clause 7.3 stated that they must be capable of substantiation. Regardless of the labelling of the price comparison chart, or the suitability of the model upon which it

was based, the Appeal Board considered that it was misleading to base the cost comparison on estimated savings and what might happen. The cost comparison was not accurate. There was no way of substantiating the material until after Prozac had come off patent and the cost each month was known. The cost of the competitor products might also change. The Appeal Board upheld the Panel's ruling of breaches of Clauses 7.2 and 7.3 of the Code.

The appeal was thus unsuccessful.

During its consideration of this case the Appeal Board noted Lilly's submission that if the Panel's ruling of a breach of the Code was upheld it would hinder pharmaceutical companies assisting their customers in financial planning through the use of predictive models. In the Appeal Board's view this was not so. If an unsolicited request came from a customer requiring such assistance then a pharmaceutical company's response would be exempt from the Code (Clause 1.2) as it would constitute a reply made in response to an individual enquiry. Such responses had to relate solely to the request, be accurate, not misleading and not promotional in nature.

Complaint received **8 September 1999**

Case completed **5 January 2000**

CASES AUTH/922/9/99 & AUTH/923/9/99 *NO BREACH OF THE CODE*

PHARMACIST v BRISTOL-MYERS SQUIBB and SANKYO PHARMA

Lipostat journal advertisements

A pharmacist complained about journal advertisements for Lipostat (pravastatin) issued by Bristol-Myers Squibb and Sankyo Pharma. There were three pairs of advertisements, each pair consisting of a one page advertisement followed by a double page spread, and each pair had a similar theme. The single page advertisement of the earliest pair, for example, bore a small photograph of a middle-age male doctor. The left hand page of the double page spread had a black and white photograph of a schoolboy in a science laboratory and the right-hand page said 'I was always good at science' and again incorporated a small photograph of a middle age male doctor. The strapline beneath the product logo said 'Prescribed by practical doctors everywhere'. The other two pairs stated respectively 'Prescribed by thoughtful doctors everywhere' and 'Prescribed by single-minded doctors everywhere.

The complainant alleged that the campaign was derogatory to the healthcare profession. The advertisements clearly implied that those doctors who did not prescribe pravastatin were not being 'single-minded' or 'practical' and exhibited a 'thoughtless' approach to patient care. This was insulting to the medical profession. Further, one of the advertisements claimed that pravastatin was the only statin that was not significantly metabolised by cytochrome P450 compared to any other statin. Without providing any details for the basis of this comparison with other statins, the prescriber was then somehow supposed to make a 'thoughtful' prescribing decision! How 'practical' was this? The complainant was also confused about the use of schoolchildren in these advertisements. Was there a suggestion that pravastatin was indicated for paediatric use? It was alleged that this series of advertisements was irresponsible and did not credit the industry.

The Panel considered that the theme was not unacceptable; each featured the transition from an ambitious child to a doctor. The Panel did not consider that the advertisements were in any way derogatory to the medical profession or that the implication could be drawn from them that Lipostat was for use in children. The evidence relating to cytochrome P450 metabolism was not given in the advertisement in question but there was no requirement in the Code that it should. The requirement of the Code was that claims should be capable of substantiation and that substantiation should be provided on request. No breach of the Code was ruled.

A pharmacist complained about journal advertisements for Lipostat (pravastatin) issued by Bristol-Myers Squibb Pharmaceuticals Limited and Sankyo Pharma UK Limited. Two pairs of advertisements were submitted, each consisting of a one page advertisement followed by a double page spread, which had appeared in GP on 27 August and 10 September respectively. The single page advertisement (ref LIP 381) of the earlier pair featured the question 'Why am I a doctor' and contained a small photograph of a middle-aged male doctor. The left hand page of the second advertisement (ref LIP 376) had a black and white photograph of a schoolboy in a science laboratory and the right hand page said 'I was always good at science' and again incorporated a small photograph of a middle-aged male doctor. Text described pravastatin as the only statin which was not significantly metabolised by cytochrome P450. The strapline beneath the Lipostat product logo read 'Prescribed by practical doctors everywhere'. The second pair had the same headline on the single page advertisement (ref LIP 381), but had a small photograph of a young female doctor, a colour photograph of a girl guide on the left hand page of the second advertisement (ref LIP 377) and on the right hand page 'I wanted to do a job where I could make a difference' and again a small photograph of a young female doctor. The strapline beneath the product logo read 'Prescribed by thoughtful doctors everywhere'. A third pair of advertisements (refs LIP

382 and LIP 378) on the same theme, not submitted but referred to by both the complainant and the respondents, featured a young male doctor and the strapline 'Prescribed by single-minded doctors everywhere' (ref Hospital Doctor, 23 September 1999).

COMPLAINT

The complainant drew attention to the journal advertisement campaign for pravastatin, which was derogatory to the healthcare profession. This series of advertisements clearly implied that those doctors who did not prescribe pravastatin, preferring to choose an alternative treatment option, were not being 'single-minded', 'practical' and exhibited a 'thoughtless' approach to patient care. On what basis were such sweeping generalisations made? The complainant thought that this was insulting to the medical profession.

One of the advertisements claimed that pravastatin was the only statin that was not significantly metabolised by cytochrome P450 compared to any other statin. Without providing any details for the basis of this comparison with other statins, the prescriber was then somehow supposed to make a 'thoughtful' prescribing decision! How 'practical' was this?

The complainant was also confused about the use of schoolchildren in these advertisements. Was there a suggestion that pravastatin was indicated for paediatric use?

This series of advertisements was irresponsible and did not credit the industry.

When writing to the companies, the Authority drew attention to Clauses 3.2, 7.2, 8.2 and 9.1 of the Code of Practice.

RESPONSE

Bristol-Myers Squibb responded on behalf of itself and Sankyo. The series of advertisements was intended to highlight certain characteristics that were common to many doctors and then to relate these to their day to day practice of medicine. In the 'single-minded' advertisement, it was suggested that it could be a single-minded determination to succeed that made a child who aspired to be a doctor achieve that goal. Since all practising doctors had succeeded in achieving their chosen profession, the implication was that all doctors were single-minded. The advertisement then pointed out that single-mindedness to practice evidence based medicine could be a reason to prescribe pravastatin, which was one of only two statins licensed and with clinical trial evidence to reduce CHD risk in post-myocardial infarction (MI) patients. There was no suggestion, either directly or by implication, that doctors who did not prescribe pravastatin were not single-minded; on the contrary, as indicated above the implication was that most doctors were single-minded.

Turning to the 'practical' advertisement, in a similar way all doctors had been through medical school and therefore would have a logical, practical mind and it was this practical approach that was used when they chose to prescribe any given medicine within a class. With regard to the 'thoughtful' advertisement, all doctors thought about the medicines they prescribed and this characteristic of thoughtfulness was therefore expressed when a doctor chose to prescribe pravastatin.

The current Lipostat campaign was extensively tested in market research to ensure that the advertisements were not derogatory to the medical profession. Forty five detailed interviews were conducted in users and non-users of pravastatin. Doctors were given a list of adjectives and asked which applied to the advertisements. Condescending, judgmental and presumptuous were on the list, but none were mentioned by more than one doctor in all of the forty five interviews. This was extremely low given the open ended and probing nature of the interviews. Accordingly to a leading agency in medical advertising testing, at least 20% of doctors normally reacted negatively to advertisements. It was agreed that should words like patronising, confrontational or aggressive spontaneously come up more than 5% of the time during the interviews, the campaign would be amended. With Lipostat there was less than 5% spontaneous use of these adjectives which the agency thought was not cause for concern. There was no difference between Lipostat users and non-users in their reactions towards the advertising campaign, and the majority of all respondents were not in any way offended by the advertisements. The words were clearly and overwhelmingly seen as applying to the medical profession as a whole, not only to Lipostat prescribers. The campaign was also presented to an advisory board of eleven consultants and general practitioners, who did not consider that it was derogatory, at all, to the profession.

The companies therefore did not believe that these advertisements were 'insulting' either to doctors or to the medical profession, as alleged by the complainant. They were therefore not in breach of Clauses 8.2 or 9.1 of the Code.

Bristol-Myers Squibb said that it was a statement of fact that pravastatin was the only statin not significantly metabolised by cytochrome P450. For most classes of medicines, the prescribing physician had the choice to use one of a number of products. While a number of factors would determine the choice of agent, the potential for medicine interactions was always an important consideration, especially when, as in the specific example used in the advertisement, the patient was already taking several other medications. There were many medicines that were metabolised by cytochrome P450, the fact that pravastatin was the only statin not metabolised by this enzyme system would be a factor to be considered when deciding which agent to use in the particular patient described in the advertisement. The reference was clearly stated and it provided details of the metabolism of pravastatin as well as the basis of the comparison with other statins.

The companies therefore did not accept the allegation made by the complainant that the advertisement provided insufficient information to influence the prescribing decision for the patient described. Consequently, there was no breach of Clause 7.2 of the Code.

Bristol-Myers Squibb stated that the use of images of children in no way suggested that there might be an indication for the use of pravastatin in children. Each advertisement was designed such that the photograph on the left hand page of the double page spread depicted, as a child, the doctor on the right. This was made clear by the text of the advertisement, some of which was in a font 10-15mm high. Furthermore, the images had been carefully chosen to ensure that the photograph of the child matched the picture of the doctor, with regard to physical appearance such as hair colour and the wearing of glasses, and also the 'age' of the photograph (hence the use of black and white photographs in the advertisements with the older doctors).

The issue of using children's images was tested during the market research and a direct quote from the market research agency stated 'At a spontaneous level, there was little or no evidence to suggest that the doctors were perceiving the children in the visuals as patients.' During the testing there was a suggestion by a few doctors that an additional advertisement might be confusing and imply the use of pravastatin in children, so this advertisement was then dropped. The remaining advertisements were not found to confuse the doctors this way.

All three advertisements specifically highlighted the use of pravastatin in post-MI patients. In addition to the above, any healthcare professional could reasonably be expected to know that MI was not a condition normally associated with children; the companies therefore failed to see on what basis the complainant could possibly infer that a claim for paediatric use of pravastatin was made. The companies did not accept that these advertisements were in breach of Clause 3.2 of the Code. For the reasons outlined above the advertisements, in the companies' opinion, were not in breach of Clauses 3.2, 7.2 and 8.2 or 9.1 of the Code. The companies also did not accept the allegation made by the complainant that the series of advertisements was irresponsible and did not credit the pharmaceutical industry.

PANEL RULING

The Panel considered that the theme in each pair of advertisements was not unacceptable; each featured the transition from an ambitious child to a doctor. The Panel did not consider that the advertisements were in any way derogatory to the medical profession or that the implication could be drawn from them that Lipostat was for use in children. No breaches of Clauses 9.1, 8.2 and 3.2 were ruled. The evidence relating to cytochrome P450 metabolism was not given in the advertisement in question but there was no requirement in the Code that it should. The Panel ruled no breach of Clause 7.2 of the Code in that regard. The requirement of the Code was that claims should be capable of substantiation and that substantiation should be provided on request.

Complaint received **9 September 1999**

Case completed **1 November 1999**

CASE AUTH/925/9/99

HOSPITAL CONSULTANT v JANSSEN-CILAG

Advertisement in eBMJ

A consultant psychiatrist complained about advertisements for Risperdal (risperidone) placed by Janssen-Cilag on the eBMJ.

The complainant alleged that the banners which had the product name and logo did not have any information relating to the generic name and the summary of product characteristics.

The Panel noted that the banner also included a statement to click for UK advertisement and prescribing information. The Panel considered that the Risperdal advertisement consisted of three linked parts; the banner, the illustration and claims (which included the non-proprietary name, next to the brand name) and the prescribing information. The banner was part of a full advertisement the whole of which needed to comply with the Code. The Panel considered that the non-proprietary name of the product should have been provided adjacent to the name of the product in the banner which, in the Panel's view, was the most prominent display of the brand name. A breach of the Code was ruled. The Panel did not consider that the breach of the Code meant that high standards had not been maintained and no breach was ruled in this regard.

Janssen-Cilag appealed the Panel's ruling. A number of arguments were put forward. The Appeal Board noted that the banner would be seen by all viewers whereas the second and third parts of the advertisement would be seen by those who had clicked on the banner.

The Appeal Board decided that the banner was part of a full advertisement. The most prominent display of the brand name was on the banner and the non-proprietary name should have appeared immediately adjacent to the brand name in the banner. The Appeal Board upheld the Panel's ruling of a breach of the Code.

A consultant psychiatrist complained about advertisements for Risperdal (risperidone) placed by Janssen-Cilag Ltd on the eBMJ.

COMPLAINT

The complainant stated that Janssen-Cilag was currently advertising its product Risperdal on the Internet. The advertisements occurred within the electronic version of the BMJ and they took the form of banners which advertised the product Risperdal and had the logo but did not, as far as the complainant could understand, contain any information which related to the product's generic name, risperidone, and its summary of product characteristics. The complainant considered that this was a fairly blatant misuse of the Internet and a breach of the Code.

When writing to Janssen-Cilag, the Authority drew attention to Clauses 4 and 9.1 of the Code.

RESPONSE

Janssen-Cilag pointed out that the site was an electronic form of the paper version of the BMJ and was intended for medical professionals as this was clearly stated on the site. It was an accepted practice that pharmaceutical advertisements appeared in the paper version of the journal and the introduction of advertising to this electronic format was simply an extension of this principle. Janssen-Cilag had worked closely with the BMJ on transferring these principles to the electronic form and together had sought guidance from the Medicines Control Agency (MCA), with the absolute intention of adhering to the Code and the Medicines Act 1968.

One consequence of the move to electronic format was the need to establish a mechanism by which the reader could choose to view an advertisement. In the paper form the reader would simply come across an advertisement by turning the pages. This was not feasible on the Internet so the use of a banner (a standard Internet device) was adopted. The Risperdal banner appeared at the top of the page. Every few seconds this banner dissolved and a message 'Click for UK advertisement and prescribing information' appeared before the original banner returned. Clicking on the banner took the viewer through to a full Risperdal advertisement. The advertisement was identical to that running in the paper version of the journal, except that due to the confined screen space and the need for legibility, prescribing information was accessed by clicking a clearly annotated button directly under the advertisement.

Janssen-Cilag submitted that the banner referred to by the complainant was merely a device by which an interested reader could access the UK Risperdal advertisement and abbreviated prescribing information and instructions as to how to do this were very clearly stated. At the point that the banner appeared it was doing no more than branding a button which allowed access to information on the product (ie advertisement and prescribing information), and no product claims were made. The advertisement contained the most prominent use of the trade name and thus the generic name appeared adjacent to this and the required prescribing information was easily accessible as stated above. Thus Janssen-Cilag considered that it had fully complied with Clause 4 in this matter.

With regard to Clause 9.1, Janssen-Cilag submitted that it had maintained a very high standard in this matter and fully recognised the professional standing of the audience. Hence it had worked closely with the BMJ, one of the most prestigious journals in the world, and had sought advice from the appropriate regulatory authority. It had also as a matter of courtesy kept the Director of the Authority informed of its actions. The use of a banner could not be

construed to be a teaser as the banner dissolved at regular intervals to clearly inform the reader of its function.

Janssen-Cilag trusted that it had convinced the Authority that the banner was not an advertisement in itself but merely a signpost to it and that it adhered to the principles of the Code.

PANEL RULING

The Panel noted that this was the first complaint about banner advertising. The Panel noted that the banner referred to by the complainant gave the product name, Risperdal, a logo and a statement to click here for UK advertisement and prescribing information. No other information about the product was given. The Panel further noted that Janssen Cilag had informed the Authority of its intentions but the Authority had not in any sense given its approval. The Authority had in fact sought guidance from the Code of Practice Appeal Board regarding electronic advertising including the application of Clause 4.1 of the Code to banner advertising in the eBMJ. The Appeal Board had decided that the position was not clear. The Code might have to be amended in light of developments in technology such as electronic advertising.

The Panel noted that there were no specific requirements for advertising in electronic journals as such although advertising in electronic media and interactive data systems was mentioned in the definition of promotion and the latter were referred to in Clause 4.3.

The Panel noted that advertisements in electronic journals must be full advertisements and the prescribing information as set out in Clause 4.2 had to be provided. Abbreviated advertisements were tightly controlled (Clause 5) and could not be included on interactive data systems. There was no objection in principle to advertisements for prescription only medicines appearing in the eBMJ even though it could be accessed by members of the public. It was no different in that regard to the paper version of the BMJ which could be purchased by members of the public or read in public libraries, even though it was primarily intended for members of the medical profession.

The Panel noted that the Code required that prescribing information be provided in advertising. The only exemptions to this were abbreviated advertisements and gifts in the form of promotional aids. The Panel did not consider that the provisions relating to gifts were relevant in any way. Both full advertisements and abbreviated advertisements had to include the non-proprietary name of the medicine or a list of active ingredients using approved names where such existed immediately adjacent to the most prominent display of the brand name in not less than 10 point bold or in a type size which occupied a total area no less than that taken by the brand name. The UK legal requirements were similar regarding the positioning of the non-proprietary name.

The Panel considered that the Risperdal advertisement consisted of three linked parts. The first part was the banner which was linked to the illustration and claims (the second part) which included the non-proprietary name adjacent to the brand name. The second part was linked to the prescribing information which formed the third part. In the Panel's view the banner was part of a full advertisement the whole of which needed to comply with Clause 4.1 of the Code.

The Panel considered that the non-proprietary name of the product should have been provided adjacent to the name of the product in the banner which in the Panel's view was the most prominent display of the brand name. It might not have been the largest in size but it was certainly the most conspicuous and was designed to catch the attention of readers. Clause 4.3 stated that when prescribing information was included in an interactive data system instructions for accessing it had to be clearly displayed. The banner included the instructions 'Click here for UK advertisement and prescribing information.' The Panel considered that the requirements of Clause 4.3 of the Code had been met.

The Panel considered that the banner failed to meet the requirement of Clause 4.2 of the Code with regard to the positioning of the non-proprietary name. A breach of Clause 4.1 of the Code was ruled as that set out the requirement that prescribing information be provided, Clause 4.2 merely defined the various elements of the prescribing information.

No breach of Clause 9.1 of the Code was ruled as the Panel did not consider that the breach of Clause 4.1 meant that high standards had not been maintained.

APPEAL BY JANSSEN-CILAG

Janssen-Cilag stated that Clause 4.1 stated that (with the exception of abbreviated advertisements and promotional aids) certain prescribing information (listed in Clause 4.2), … must be provided in a clear and legible manner in all promotional material for a medicine.' Amongst the prescribing information to be provided as per Clause 4.2 was 'the name of the medicine (which may be either a brand name or a generic name). In addition the non-proprietary name of the medicine or a list of the active ingredients using approved names where such exist must appear immediately adjacent to the most prominent display of the brand name in not less than 10 point bold or in a type size which occupies a total area no less than that taken by the brand name.'

Janssen-Cilag stated that the eBMJ website, in terms of its commercial use of the brand name Risperdal, consisted of three linked screens (or electronic display pages), which had to be accessed in order (first through third Risperdal screens). The first of the Risperdal screens displayed the brand name (on a subsidiary banner at the top of the screen) without the proprietary name, while the second Risperdal screen showed the brand name with the non-proprietary name under it. The Panel opined that the non-proprietary name should have been immediately adjacent to the brand name on the first Risperdal screen, since it was this screen which, in the Panel's view, gave the most prominence to the brand name when compared with the other screens which displayed the brand name.

The Panel therefore considered that the banner (on page 1 of the Risperdal electronic display) failed to meet the requirement of Clause 4.2 'with respect to the positioning of the non-proprietary name', thereby leading to a ruling of a breach of Clause 4.1.

Argument One

The brand name 'Risperdal' found on screen dump 1 (on the first Risperdal electronic display page) was not more prominent than the brand name found on the second Risperdal electronic display page.

The Panel noted in its decision that: 'The Panel considered that the Risperdal advertisement consisted of three linked parts …. The Panel considered that the non-proprietary name of the product should have been provided adjacent to the name of the product in the banner which in the Panel's view was the most prominent display of the brand name'.

In the Panel's view, the case turned simply on the issue of whether the smaller Risperdal brand name (cum logo) found in the box which constituted 'screen dump 1' (on the first Risperdal e-display page) was thought to be more 'prominent' than the larger Risperdal brand name (cum logo) found on the second screen, such that the non-proprietary name should have been placed on the former screen instead of the latter. The Panel's decision was based upon its subjective interpretation of the meaning of 'prominence'. Ultimately it ruled that the generic name belonged on the first of the e-display screens since this was where it thought the most prominent brand name was on display; a breach of Clause 4.1 was thus ruled. Had the brand and non-proprietary name both appeared on the first screen then the Panel would have not have ruled a breach.

Janssen-Cilag disagreed with the Panel's ruling of a breach. It argued that the ruling was 'unsafe' since it was a diversion away from the previous standard of 'size' which had heretofore been the major deciding factor governing 'prominence'. Moreover, the Panel's announced new standard as to 'conspicuousness' to help it determine the prominence of screen-based advertising had been applied in a confused manner. Janssen-Cilag believed that it was on the second display screen which mentioned Risperdal that the most prominent use of the brand name might be found.

The eBMJ website contained numerous pages overall; it changed over the course of time, even within one on-line period of viewing. So that the Appeal Board and Janssen-Cilag could discuss, initially in a paper-based presentation of the evidence, the electronic pages concerning Risperdal upon which the case was based, it would be best if Janssen-Cilag were to adopt similar terminology that could then be used to review the screens. Below, Janssen-Cilag set forth its terminology and used it to 'walk' the Appeal Board through the process of viewing the electronic display at issue.

Firstly, no advertisements for the promotion of medicines were to be found on the home page of the 'current issue eBMJ' website. To proceed the viewer must enter into one of the several major divisions of the website (for example: 'Current issue', 'Search/Archive', 'Collected resources,' etc – although not all of the subdivisions granted access to advertisements for prescription only medicines).

Once into one of the divisions of the eBMJ website which allowed for access to advertisements, banners might be found which changed over time; however, the underlying second screen of the eBMJ site remained in place while any banner changes occurred. A banner might go through various changes (ie 'screen dumps').

The first electronic display page which mentioned Risperdal, screen dump 1, showed that the brand name Risperdal and the product logo were found in the 'Table of Contents' subdivision (of the 'Current issue' division) of the electronic journal. The name Risperdal and the brand's logo could be found in a small box located above a box marked 'Table of Contents'.

Screen dump 1 then changed automatically into:
screen dump 2 which stated 'Click for'; this second dump then metamorphosed into
screen dump 3 which stated 'UK Advertisement'; this third dump then changed into
screen dump 4 which stated 'and Prescribing Information'.

The four screen dumps (banners) on this screen of the eBMJ website went through a continuous cycle of approximately 5 seconds' duration, with each separate banner being shown in turn and by screen dump numerical order, before the process began again. All four screen dumps were located on the first electronic display screen to mention Risperdal; the first display screen, which underpinned the banners, remained the same as the screen dumps went through their rotation.

Placing the mouse over any of the screen dumps 1-4 brought up a 'hand pointer' icon which told the reader, via a yellow advisory box, that an 'Advertisement for health professionals' would follow – if the instructions to 'Click' were followed. Clicking on any of screen dumps 1, 2, 3 or 4 brought up the second screen of the Risperdal electronic display (ie the third screen into the overall eBMJ website) which contained the elements which actually constituted an advertisement (brand and generic names, illustration, product claims, etc).

This second Risperdal display screen consisted of a Risperdal advertisement, exactly as one would see it in the print version of the BMJ (except that the abbreviated prescribing information [API] had been moved to a third and final Risperdal screen, due to space consideration). This second screen contained screen dump 5; this consisted of an illustration (image of a woman), copy and product claims/indications. At the (bottom) outer edge of this initial screen of the electronic analogy to page one of a print/paper version of the Risperdal advertisement could be found a 'forwarding' arrow which let the viewer access the API (as per Clause 4.5 of the Code). This arrow was labelled 'Click for UK Prescribing Information.' Moreover, just as in the case of the first Risperdal screen with its screen dumps 1-4, putting the computer mouse over the 'Click for next page'

mechanism/forwarding arrow brought up another 'hand icon' which notified the user, again via a little yellow advisory box, that 'Prescribing Information' would follow the forwarding – if the arrow was clicked.

The Panel had characterised the Risperdal banner on the first screen of the electronic display to mention the Risperdal brand name (ie screen dumps 1-4) as being the most 'conspicuous' part of the entire Risperdal display (ie it was 'designed to catch the attention of readers,' as the Panel stated), notwithstanding the fact that (again, in the Panel's words) '[i]t might not have been the largest in size.' It should first be noted that 'conspicuous' was not only not defined by the Code, but that it did not necessarily equate with what was the recognised standard – 'prominence'. Unfortunately Janssen-Cilag was at somewhat of a loss in this appeal, since the Panel had not elucidated upon what feature(s) the banner had had designed into it which gave it the feature of being 'conspicuous'.

It should next be noted that the whole object of promotion was to get the attention of the intended subject. This was doubly important when the actual advertisement (brand name, generic name and product claims/indications) lay underneath the initial banner. If the advertiser did not 'catch the attention of readers' (to use the Panel's own phrase), then no promotion could be obtained. Unlike the paper version of the BMJ, where flicking through an issue from front to back allowed access to all pages, a reader of the eBMJ must be shown where to click in order to access a certain page, otherwise the page would never appear in plain view. As Janssen-Cilag stated in its initial answer to the complaint, this difference in the medium necessitated the use of a banner(s), a standard Internet device. A certain degree of 'catching the eye of the reader' was therefore warranted but Janssen-Cilag did not believe that the degree of eye-catching on the first Risperdal screen out-weighed the prominence of the Risperdal name on the second screen.

Janssen-Cilag had assumed for the purposes of its appeal that it was the rotation between the various separate elements of the banner (ie, the four individual screen dumps) that constituted the 'eye catching' feature upon which the Panel had focused its attention. However, it was only screen dump 1 being used in conjunction with screen dumps 2-4 (giving a feeling of movement) that allowed screen dump 1 (the brand name) to have any degree of 'conspicuousness'. The Panel mistook the notion of the 'conspicuousness' of the banner as a whole with the Code requirement that the non-proprietary name be (immediately) adjacent to that display of the brand name that was the most prominent.

Even with the continued repetition of screen dumps 1-4 through some sequencing mechanism, these four screen dumps combined still constituted but a very small part of the plethora of other materials which occupied the same electronic display page, which other materials were equally accessible by clicking highlighted or emboldened portions of the screen text, directional arrows and the like. At the time of the complaint, screen dumps 1-4 were listed on the same page with the Table of Contents, which itself was capable of being scrolled down several pages and which contained a wealth of information as to the contents of the site.

It was the case, though, that the Code standard was not based on a debate as to whether a series of screen dumps as a whole gave a feeling of conspicuousness; rather the Code stated that the non-proprietary name should appear (immediately) adjacent to the most prominent display of the brand name in promotional material. Seen in this light, screen dump 1 (the brand name 'Risperdal') was off the screen for approximately three-quarters of the time, since it was only one of four banners. When it was on the screen, it had to compete with other material for attention; this included its sister banners and the rest of the 'clickable' entry points into the website which continued in view while the screen dumps continued through their cycle. Screen dump 1 amounted to a fairly innocuous display of the brand name – when compared to the larger (but stationary) display of the brand name on screen dump 5 (located on the second Risperdal screen).

It should be noted that not only was the actual advertisement found on the second screen (ie screen dump 5) as a whole larger than screen dumps 1-4 which made up the first Risperdal screen, but the Risperdal brand name was bigger on screen dump 5 than on screen dump 1. Finally, the Risperdal names/logo box was a larger proportion of the overall screen information found on the secondary screen than was screen dump 1 *vis-à-vis* the screen on which it was found.

However, if one was allowed to take into consideration the whole of a Risperdal display on a page (as it appeared that the Panel did in its evaluation of 'conspicuousness') and not just focus on the prominence of only the brand name then Janssen-Cilag still believed that the second screen of the Risperdal display was more prominent than the first. First, it should be noted that the image and text of the advertisement section of the display (screen two of the display) constituted a very striking ('eye catching') combination. These elements, additionally, told a story and most probably grabbed and kept the reader's attention more than screen dumps 1-4 which were merely instructions as to how to access the story. It might also be said that the repetition of screen dumps 1-4 soon became wearisome.

The elements of the advertisement found on screen dump 5 (image/illustration, product claim/indication and in particular the product's brand name) were more 'prominent' (the Code standard) than those of screen dump 1 (or even screen dumps 1-4 taken together) since these elements took up the entire second screen of the Risperdal display without any competition for attention; the second screen on which the brand name appeared was, unlike the first screen on which the brand name appeared, wholly dedicated to the product. Finally, all the elements of the advertisement – but especially the brand name (cum logo) remained on the screen the entire time.

Because of the above factors Janssen-Cilag argued that its interpretation of what constituted 'prominence'

was reasonable and, furthermore, consistent with the Code's requirements. The non-proprietary name was therefore properly placed on screen dump 5 (the second screen of the Risperdal display) and a violation of the Code was wrongly adjudged.

Under the Panel's ruling, the use of the non-proprietary name on screen dump 1 satisfied Clause 4.2 of the Code of Practice (generic name to be placed immediately adjacent to the most prominent display of the brand name). The non-proprietary name therefore did not have to appear again in the advertisement. Following this logic to its natural conclusion, the appellant company wondered how the Panel would react if Janssen-Cilag then chose to remove the non-proprietary name from the second Risperdal screen (screen dump 5). This scenario, Janssen-Cilag believed, would lead to an anomalous situation since the electronic version of advertisement would no longer mirror the advertisement as it appeared in the print version of the BMJ; it was this mirroring which had been the *sine qua non* for the Medicines Control Agency (MCA) allowing the BMJ to proceed with web advertisements! The MCA's logic was even alluded to in the Panel's review of the recent advent of advertising in electronic journals when it noted that the rationale given for permitting it was that it was 'no different to the paper version of the BMJ.' The Panel's ruling appeared confused; any concurrence by the Appeal Board in the Panel's ruling would result in upholding an illogical ruling.

Therefore a decision as to 'prominence' should be treated as if one were weighing up the merits of the same advertisement in the print BMJ. To say that the non-proprietary name should be placed in the Risperdal name/logo screen dump on the first display page rather than the second display page was not only arbitrary given the lack of specific established standards as to web advertising (a situation admitted to by the Panel) – but it was also at odds with government regulations as to the advertisement of medicines and with general guidance given by the MCA (see also Argument Four, below).

Argument Two

The first screen of the electronic display to list the brand name, Risperdal, was not part of the Risperdal advertisement.

The Panel's decision stemmed from the premise that the 'Risperdal advertisement consisted of three linked parts'. Janssen-Cilag disagreed strongly with this characterisation of the advertisement.

Janssen-Cilag would respectfully point out, firstly, that the complainant initially pre-judged the issue by the language used in his complaint. He stated that the Risperdal advertisement 'takes the form of banners'. He thus equated the entire three screens with 'banner advertising'. Unfortunately the Panel continued along these lines by stating that 'this was the first complaint about banner advertising' that had reached it. With this notion in mind, the Panel's logic followed a path which invariably led to the finding of a Code violation. This was most odd since the conclusion did not follow from one of the major premises which underlined the Panel's initial discourse on web advertising – that was, the fact that permission to engage in e-advertising stemmed from the MCA's view that no harm was done when the substance of the e-advertisement was based on the print version which was available for all to see.

This was not to say that a banner could never be an advertisement as 'banner advertisements' did exist; nor was it the case that a banner intended to be an advertisement could never fall foul of the Code in some way. However, as to the instant case, screen dumps 1-4 (the four initial banners of the primary screen) were not and were never intended by either Janssen-Cilag or by the publishers of the eBMJ to constitute an advertisement by themselves as they had few of the elements of a promotion; more so, they were not meant to be part of an advertisement in conjunction with the other two (secondary and tertiary) screens.

In the instant case both Janssen-Cilag and the editors of the eBMJ viewed the first screen to mention Risperdal with its banner/four screen dumps as a web portal into the actual advertisement which was found on the next two screens (the image/text of screen dump 5, followed by prescribing information). The second screen could only be accessed through the first Risperdal screen and specifically through this latter screen's four screen dumps. Moreover, Janssen-Cilag considered that the Authority should also similarly view the breakdown of the screens into these two categories of portal banners plus advertisement pages.

Janssen-Cilag and the publisher had endeavoured to see to it that the electronic advertisement mirrored, as closely as possible (given the different media used), the hard copy advertisement of the print issue of the BMJ. Given that the banner was merely a tool to reach this electronic analogue of the print version, then the initial screen dumps (1-4) which included the Risperdal brand name but not the generic name did not need to comply with Clause 4.2 of the Code in terms of also listing the non-proprietary name outside of the advertisement.

If it were to be the print version of the Risperdal advertisement that was being scrutinised by the Panel and the Appeal Board, Janssen-Cilag was confident that this version contravened no clauses of the Code. The eBMJ version, found on the secondary and tertiary Risperdal screens, was as exact a replica of the Risperdal print advertisement as it was humanly possible to achieve, given the fact that a VDU screen was not a piece of paper. A photograph (image/illustration), headline and strapline, text and product claims appeared on the secondary Risperdal screen (screen dump 5) – along with the most prominent listing of the brand name (and hence an accompanying non-proprietary name) – while the API appeared on the tertiary Risperdal screen (screen dump 6).

Not only was this the type of advertisement that the 'man on the Clapham omnibus' was familiar with, but all the elements of an advertisement which was in accord with the Code were contained in these two screens.

The banner in its totality was simply a set of facts: an advisory as to what was to come on the next screen ie

an advertisement which was intended for UK health professionals, and instructions for 'turning to the correct electronic' page (Click here for the advertisement).

Janssen-Cilag argued that the banner on the first Risperdal screen was not a promotion within the scope of the Code. Rather it constituted a 'factual, accurate, informative announcement' or 'reference material' under Clause 1.2 of the Code. This banner (screen dumps 1-4) merely announced the 'what', 'when', 'where' and 'how' as to the actual advertisement (in the way of a table of contents or reference list for advertisements). There was no need to further spell out the analogies to the print version.

The banner in question was a 'banners for accessing advertisements' and did not constitute in and of itself a 'banner advertisement'. Surely this must be the method that should be adopted so that persons browsing the eBMJ did not come upon promotional material by chance. Janssen-Cilag would argue strongly that neither the Risperdal advertisement nor the introductory banner for accessing the advertisement failed to meet the requirements of Clause 4.2; nor did they actively contravene Clause 4.1 of the Code.

Finally, it would appear that the MCA would agree with this analysis of screen dumps 1-4 as constituting only a mechanism by which the reader's attention was drawn to the actual advertisement. (See Argument Four).

Argument Three

The Panel's decision was an arbitrary ruling as to a technical point in the Code which did not address the issue raised by the complainant.

The complainant stated as follows:

They [Janssen-Cilag] are currently advertising their product Risperdal on the Internet. The advertisements occur within the electronic version of the BMJ and they take the form of banners which advertise the product and have the logo but do not, as far as I can understand, contain any information which relates the product's generic name risperidone and its summary of product characteristics …

The complainant took issue with the 'fact' that 'as far as [he] can understand' the '*banners* [Janssen-Cilag's emphasis as to the plural form] do not … contain any information which relates the product's [Risperdal's] generic name risperidone and its summary of product characteristics [SPC].'

It could be deduced from the complainant's use of the plural form of the word 'banner' and the non-proprietary name (risperidone) that the complainant successfully 'navigated' from the primary screen of the Risperdal electronic display to the secondary screen (ie as far as two pages into the eBMJ Risperdal display). It then seemed apparent that the complainant missed the arrow on the second page of the electronic display which 'turns the page' to Page 3 ('Click here for UK Prescribing Information'), where the Risperdal abbreviated prescribing information was set forth. Either that or, with due respect, the complainant appeared not to have worked out how the eBMJ website operated.

The Panel's announced decision was one for a case where the reader complained that he missed the non-proprietary name of the medicine being advertised because it was not placed next to the most prominent display of the brand name. In the instant case the complainant himself stated that he was indeed able to relate the brand name (Risperdal) to the non-proprietary/generic name (risperidone). His complaint was that the advertisement did not permit him to relate the generic name risperidone to the summary of product characteristics. This was clearly incorrect since the tertiary screen of the Risperdal display was dedicated solely to setting forth the API.

There was probably little that the Panel could do in terms of the complainant's incorrect assertion that the advertisement did not permit access to product information. The 'fact' was simply that the complainant missed the large arrow at the bottom of the secondary Risperdal screen which then allowed the reader access to the tertiary screen. As could be seen in screen dump 5, the caption to the arrow stated 'Click here for Prescribing Information'. This page turning device had itself been made more prominent by the fact that placing the mouse arrow over the page forwarding button brought up a 'hand' icon which was attached to a yellow rectangular box in which the advisory caption 'Prescribing Info' appeared.

The Panel's ruling did nothing which aided the resolution of the actual complaint because the actual complaint was not addressed, although not much could be done when a viewer failed to go to a continuation of an advertisement, which continuation was located 'overleaf'. Such continuations onto another page of an advertisement were indeed permitted under Clause 4.5 of the Code with respect to prescribing information. This clause stated, in part, that '[i]n the case of a journal advertisement [the eBMJ being an electronic version of the printed BMJ], where the prescribing information appears overleaf, a reference to where it can be found must appear on the outer edge of the initial page of the advertisement in at least 8 point type.' The complainant failed to note the reference (on what Janssen-Cilag considered to be the 'initial page' of the e-advertisement), which reference was located on the bottom right (outer edge) of the screen.

This case was purely and simply an instance where the complainant failed to take note of a proper reference to the API appearing overleaf. The Panel had firstly misread the complaint and then, through a very convoluted process of logic, turned the issue into one of whether the smaller Risperdal name located on screen dump 1 was more or less 'prominent' than the larger brand name located on screen dump 5. The Panel had made its decision based upon some unknown operational mechanism based around the properties of 'conspicuousness' (the elements of which were not set forth).

The Panel owed both the complainant and Janssen-Cilag the duty to answer the complaint before it. The decision, as enunciated by the Panel was not focused

on the allegations and merits of the case as brought by the complainant.

While Janssen-Cilag would never say that the Panel should be enjoined from taking up other violations that it uncovered during its investigation of a complaint, the present ruling both failed to answer the controversy at hand and then went off on a complete tangent to deal with specious claims of its own making, using non-Code standards in the process. The Appeal Board should correct this situation and this was simply done. A copy of the appellant's brief in this matter, when sent to the complainant, would provide adequate instruction as to how the initial page of the e-advertisement (which included both the brand name and the generic name) was connected to an 'overleaf' page which set forth prescribing information akin to the summary of product characteristics.

Argument Four

The medical journal website advertisement and the means to draw attention to its existence were approved by the MCA's policy manager for advertising.

The Panel had noted the UK legal requirements were similar (to those of the Code) regarding the positioning of the non-proprietary name.

Janssen-Cilag was conscious of the precedence-setting nature of placing the first advertisement for a prescription only medicine on an 'open-access' (that was, open to the public without any security provision such as a password) website. Janssen-Cilag was concerned that this e-advertisement and the means to access it might be misconstrued as being an attempt to promote its product to the public. For this reason it entered into dialogue and correspondence with the appropriate department of the MCA, the Post-Licensing Division. The policy manager for advertising was shown an example of the prototype advertisement section of the website, including not only the two advertisement screens themselves but also the banner by which the portal drew attention to itself and through which the advertisements were accessed. The MCA voiced no objection either as to the two advertising screens themselves or to the manner in which the four banners were arranged in rotation and through which the advertisement was accessed. Indeed it found the arrangement satisfactory, stating:

'We have considered carefully both the advertisement and the mechanisms by which you intend to draw the readers attention to the presence of the advertisement; both are considered acceptable.'

Argument Five

Fundamental fairness mandated that the good faith efforts on the part of Janssen-Cilag in setting up the first UK medical journal website advertisement for a prescription only medicine should not lead to a breach of the Code.

Assuming that the Appeal Board were to reject the four arguments on appeal which Janssen-Cilag had set forth above, Janssen-Cilag would ask the Board to overrule the Panel based on the concept of 'fundamental fairness'. This doctrine would decree under these circumstances that one should not be held responsible for violating a requirement which had not, as yet, been announced.

This argument was different from the 'I was unaware of the law' argument. The Panel had itself noted that this case was one of 'first impression' as to web advertising. While analogies to some parts of the existing Code could perhaps be drawn, as the Panel did when it referred to Clause 4.3 in its decision, other clauses might have to be altered (such as those referring to font size) or new clauses drafted as to web advertisements. There was precedent for such a concept of 'fundamental fairness' having already been applied. The 1998 edition of the Code began with a statement that '[t]his edition of the Code of Practice comes into operation on 1 January 1998. During the period 1 January 1998 to 31 March 1998, no promotional material or activity will be regarded as being in breach of the Code if it fails to comply with its provisions only because of requirements which this edition of the Code newly introduces.' Therefore, how much more so was the necessity to apply such a doctrine when new provisions as to the Internet had not as yet been introduced.

When there was already a print provision which might apply through the use of reasoning by analogy as to the requirements of the Code, then advertisers should not be found in breach of the Code when there had been a good faith effort to comply. The mere fact that the Authority had the power to set forth and then enforce its own *ex post facto* interpretation of the technicalities of how the e-advertisement should have been arranged on the screen did not mean that the Panel should indeed do so. This was even more the case when the two arguments could be said to stand in equipoise. Even if the Appeal Board also thought that the non-proprietary name should have been joined to the primary screen rather than to the secondary screen because the former screen had a marginal advantage in terms of prominence, that decision should not be enforced in light of the fact that no Internet standards had been enunciated by the Authority.

Summary

In summation, at the very least, the doctrine of 'fundamental fairness' called for a ruling in favour of Janssen-Cilag as to the issue of 'prominence' raised by the Panel and upon which the Panel ruled; this was because Janssen-Cilag made a good faith effort to comply with the Code in a situation where the requirements had not been made clear. There was precedent for such a decision by the Authority. At worst the Appeal Board was dealing with a case of 'equipoise' in terms of weighing up the countervailing arguments between the Panel and the company; in the case of a tie, the company was entitled to avoid being found in breach of the Code.

As to the complaint from the consultant psychiatrist, which complaint was not addressed by the Panel, Janssen-Cilag considered that the Appeal Board could

make a determination in place of the Panel. Based on the complainant's own words, there was a case of error on his or her part. The API (tertiary screen) was indeed accessible from the secondary screen which the complainant appeared to have reached. S/he evidently somehow missed the forward button on the outer edge of the screen. Readers could also overlook an API overleaf, but this scenario was not always attributable to a fault by the advertiser. The forward button was itself prominent and came with a hand icon to further aid the process of accessing the API. Janssen-Cilag was not at fault in such a circumstance where the complainant missed the overleaf or did not know how the technology worked, even with an electronic prompt.

APPEAL BOARD RULING

The Appeal Board noted that this was a difficult case. Companies were still finding their way with electronic advertising using a Code which was written mainly for printed material although there were references to audio-visual materials and to interactive data systems. The Code applied whatever the media used.

The Appeal Board decided that a working party should be established as a matter of urgency to look at the Code in relation to advertising in electronic journals.

The Appeal Board considered that screens 1-6 constituted one Risperdal advertisement consisting of three linked parts. The first part was the banner which was linked to the illustration and claims (the second part) which included the non-proprietary name adjacent to the brand name. The second part was linked to the prescribing information which formed the third part. The Appeal Board noted that the banner would be seen by all viewers whereas the second and third parts would only be seen by those who had clicked on the banner. In the Appeal Board's view the banner was part of a full advertisement the whole of which needed to comply with Clause 4.1 of the Code.

The question to be decided was which was the most prominent display of the brand name. The Appeal Board noted the New Shorter Oxford Dictionary definition of prominent 'Jutting out or protruding from a surface. Standing out so as to catch the attention; conspicuous...'.

The Appeal Board decided that in this case the most prominent display of the brand name was on the banner and as a consequence the non-proprietary name should have appeared immediately adjacent to the brand name in the banner. The Appeal Board upheld the Panel's ruling of a breach of Clause 4.1 of the Code. The appeal was unsuccessful.

Complaint received **15 September 1999**

Case completed **10 January 2000**

CASE AUTH/926/9/99

YAMANOUCHI PHARMA v ABBOTT

Hytrin detail aid

Yamanouchi Pharma complained about a detail aid for Hytrin BPH (terazosin) issued by Abbott and entitled 'A wee rest from nocturia'. Hytrin BPH was indicated for the symptomatic treatment of urinary obstruction caused by benign prostatic hyperplasia (BPH). Yamanouchi supplied Flomax (tamsulosin).

Yamanouchi alleged that a bar chart on a page headed 'Hytrin BPH: Setting standards for BPH symptom relief' was misleading and disparaging because it gave the impression that tamsulosin was inferior and there was no evidence to support that. The bar chart compared percentage symptom improvement scores over placebo of alfuzosin (one bar; 13%), tamsulosin (four bars; 9-14%) and Hytrin BPH (seven bars; 9.5-31%) but the data were from separate studies which were not even similar. The Panel considered that the page invited the reader to directly compare data from non-comparative studies and implied that it was appropriate to do so. There was no valid basis for comparison of the studies in this way. Further, the page gave the impression that Hytrin BPH was superior to other agents, which was not supported by the evidence. The Panel considered the page misleading as alleged and ruled a breach of the Code. Breaches were also ruled because the bar chart gave a visually misleading impression of the differences between the products and was disparaging.

Yamanouchi alleged that the titration doses used in the terazosin studies were not in accordance with its summary of product characteristics (SPC) which stated that treatment should be initiated using the Hytrin Starter Pack. The Panel noted that the SPC only required strict compliance with the starting dose of 1mg, the requirements in relation to subsequent dosing were less precise and could be tailored to individual patient response. In each of the Hytrin BPH studies referred to in the bar chart a starting dose of 1mg was used, thereafter the dose was titrated at varying rates. Whilst the titration rates at issue were different to the starter pack, the Panel did not consider them to be inconsistent with the SPC and ruled no breach of the Code in that regard. It was likely that doctors would use the starter pack for most patients and the efficacy results presented were not necessarily relevant to these patients. The Panel considered that the use of the efficacy data without further explanation was misleading and ruled a breach of the Code.

A page headed 'Nocturia: Have a good night with Hytrin BPH' bore a bar chart which showed the percentage improvement in nocturia seen in separate published studies with a bar each for Hytrin BPH (43%), tamsulosin (29%), alfuzosin (18%) and indoramin (19%). Yamanouchi alleged that the bar chart was designed to mislead the reader into believing that Hytrin BPH had a much more significant effect when there was no evidence to support this claim. The Panel considered that its earlier ruling was relevant. Data from separate non-comparative studies had been presented. In the opinion of the Panel the bar chart would invite the reader to compare the percentage improvement in nocturia for each medicine. The Panel considered that the methodology of the studies differed markedly in terms of duration of treatment and statistical analysis such that the comparison was unfair. The Panel considered the bar chart misleading and disparaging and breaches of the Code were ruled. Yamanouchi alleged that the titration schedule in the cited data was not that in the Hytrin BPH SPC. The Panel ruled that this was misleading and in breach of the Code. The titration schedule was not inconsistent with the SPC and no breach was ruled in that regard.

On a page headed 'Hytrin BPH: Tailoring treatment for individual patient management', beneath the sub-heading 'Treatment is not restricted by a single, licensed dosage regime', a bar chart compared the efficacy of Hytrin BPH 5mg and 10mg, showing that 67% and 79% of patients respectively obtained ≥ 30% symptom improvement. Yamanouchi alleged that Abbott's data did not support the apparent hanging comparison 'Tailoring of dose allows more patients to achieve significant relief' which appeared beneath the bar chart. Yamanouchi presumed that this was intended to mean that more patients obtained significant relief than if the dose was not tailored but the study cited contained no group whose dose was not tailored. Further, without the placebo group results, a p value or patient numbers, it was impossible to judge the clinical benefit and was therefore not a fair or balanced presentation of the data. The Panel noted that the study in question was a multi-centre placebo-controlled randomised dose titration study of once a day administration of terazosin in the treatment of the symptoms of BPH of 177 evaluable patients. The Panel noted Abbott's submission that the abstract presented a sub-analysis of the main study. No placebo results were provided and no p values stated. The Panel considered that in the absence of this information it was thus not possible to judge the clinical significance of the data. The Panel considered that the bar chart gave the impression that there was an important difference in the percentage of patients with ≥30% symptom improvement obtained at 10mg and 5mg Hytrin BPH and that this difference was of statistical significance. The bar chart thus gave a visually misleading impression of the data and a breach of the Code was ruled. The Panel considered that neither the statement 'Tailoring of dose allows more patients to achieve significant relief' nor the bar chart were substantiated by the study as it was not possible to determine the significance of the results obtained. A breach of the Code was ruled. The Panel did not consider the phrase to be a hanging comparison, as alleged, and no breach of the Code was ruled in that regard. The Panel considered that the reader would reasonably assume tailoring to mean prescribing the most appropriate dose for the patient depending on therapeutic response. The Panel noted that in response to the request for substantiation Abbott had provided the abstract. Abbott had not, therefore, provided

substantiation and a breach of the Code was ruled in that regard. Yamanouchi alleged that as before the titration schedule in the cited data was not that in the Hytrin BPH SPC. The Panel ruled that this was misleading and in breach of the Code. The titration schedule was not inconsistent with the SPC and no breach was ruled in that regard.

A page headed 'No clinically significant effect on blood pressure in normotensive and controlled hypertensive patients' bore, beneath the sub-heading 'Hytrin BPH '… produced no clinically significant mean blood pressure changes in patients with a normal baseline DBP' ', a chart showing its effects on diastolic blood pressure (DBP) in normotensive and controlled hypertensives with BPH. Yamanouchi alleged that the page was misrepresentative in that the reader was led to believe that Hytrin BPH could be prescribed without risk of hypotension to a treated hypertensive patient without any specific caution or dose adjustment, which was contrary to the SPC. The Panel considered that the page gave the impression that Hytrin BPH treatment was not associated with an effect on blood pressure in normotensive or controlled hypertensive patients which was not so and inconsistent with the Hytrin BPH SPC. A breach of the Code was ruled. The claim 'Hytrin BPH '… produced no clinically significant blood pressure changes in patients with a normal baseline DBP' ', though a quotation from a paper, was alleged by Yamanouchi to be contrary to the many warnings in the SPC. The Panel considered that one of its earlier rulings was relevant with regard to statements in the SPC regarding postural hypotension in some patients and the overall impression of the page. The Panel considered that the quotation in this context underlined the general impression that Hytrin BPH was free from problems with blood pressure changes which was not so. A breach of the Code was ruled. Yamanouchi stated that the chart was referenced to a study which was a combined analysis of six placebo controlled studies, certain of which were inconsistent with the SPC and the impression gained from the chart was that there were no problems with hypotension. The Panel considered that its earlier rulings about differences in titration regimes and about the side-effect profile and the impression that there were no problems with hypotension and breaches of the Code were relevant. Breaches were also ruled because patient numbers should have been given as the small patient population was of relevance to the failure to achieve statistical significance. The chart was misleading and unbalanced.

Yamanouchi also alleged that the detail aid was in breach of Clause 2 of the Code. The Panel noted that a ruling of a breach of Clause 2 was a sign of particular censure and was reserved for such circumstances. The Panel considered that it was very important that companies were clear and accurate about studies presented in promotional material. The Panel was concerned about the ruling of breaches in relation to safety data. However, on balance, the Panel did not consider that the material was such to merit a ruling of a breach of Clause 2.

Yamanouchi Pharma Ltd complained about a detail aid entitled 'A wee rest from nocturia' (ref PXBPH1999050) for Hytrin BPH (terazosin) issued by Abbott Laboratories Limited. The detail aid was used by the Abbott sales force to promote to consultant urologists and their senior colleagues. Hytrin BPH was indicated for the symptomatic treatment of urinary obstruction caused by benign prostatic hyperplasia (BPH). Yamanouchi supplied Flomax (tamsulosin).

A Page 3 headed 'Hytrin BPH: Setting standards for BPH symptom relief'

This page featured a bar chart which showed the percentage symptom score improvement over placebo of alfuzosin (one bar; 13%), tamsulosin (four bars; 9-14%) and Hytrin BPH (seven bars; 9.5-31%). Each bar represented the results obtained in separate studies using licensed maintenance doses. The relevant study, dosage and patient population was stated on and above each bar. The actual percentage symptom score improvement was not given on each bar. This was obtained from the y axis. A sub-heading stated 'Attributable improvements above placebo in separate, non-comparative studies', and text beneath the table stated 'How the 'selective' alpha blockers compare in published randomised placebo-controlled double-blind clinical studies'. A footnote described the different symptom score methods employed in the non-comparative studies; American Urology Association Symptom Scoring (AUA), Boyarsky and The International Prostate Symptom Score (IPSS).

A1 The comparison

COMPLAINT

Yamanouchi alleged that the page presented a striking visual which gave one clear message to doctors, that Hytrin BPH worked 2-3 times better than either alfuzosin or tamsulosin. The data contained in this visual were all from separate studies, which were not even similar. In this regard Yamanouchi referred to a table it had produced which compared symptom scoring method, patient population, length of treatment, placebo response and compatibility of dosing with the summary of product characteristics (SPC) for each of the studies featured in the bar chart.

As Abbott itself had acknowledged to Yamanouchi, there were no published comparative data. Nevertheless, the page was overtly inviting comparison, 'How the 'selective' alpha blockers compare …'. Yamanouchi had confirmed that Abbott intended the comparison to be made in order 'to allow appropriate prescribing decisions to be made by physicians.'

Yamanouchi stated that the comparative table it had provided clearly showed that:

a) Different symptom scores were used to demonstrate efficacy (a point which Abbott partially acknowledged in tiny print at the bottom of the page of the detail aid). Depending on what symptoms were scored and how the different symptoms contributed to the overall score, even the same product would give different percentage

improvements over placebo using different scoring methods.

b) Symptom score at entry showed marked variation as could be seen from the reputedly most effective terazosin study (Brawer *et al* (1993)), compared with the Abrams *et al* (1995) study with tamsulosin, both using the Boyarsky scoring method, or the terazosin Lepor *et al* (1996), (AUA ≥ 8) compared with tamsulosin Lepor *et al* (1998), (AUA ≥ 13). Again, neither the same product, nor equivalent products could necessarily be expected to show the same degree of efficacy in severe and less severe patient groups.

c) Length of treatment – apart from Lepor *et al* (1992), the terazosin studies were long-term (24-52 weeks) whereas the other studies were 4-13 weeks in duration.

d) Placebo responses – the placebo response in these studies showed a marked variation, approaching threefold. A study with a 10.6% placebo response, Brawer *et al* (1993) was in no way comparable to one with a 28% placebo response Lepor *et al* (1998). Again, even the same product would produce different results in such different patient populations.

Yamanouchi alleged that this presentation was hardly the 'scientific review' that Abbott asserted it to be.

In the selling situation, the doctor was influenced by first, visual impressions. He had no time to ask the detailed questions which were necessary if he was to make an informed judgement of the validity of the visual. He relied on the integrity of the industry, governed by the Code, for this impression to be supported by sound unbiased, scientific fact. Even if he noted, or had drawn to his attention, the fact that these were non-comparative studies, he would consider them appropriate to be compared, as otherwise no comparisons should be made.

It was intriguing to note that in inter-company correspondence Abbott referenced and enclosed, as justification for such a flagrant abuse of non-comparable data, an abstract which stated, 'there are no dramatic differences in the efficacy and safety of currently available alpha-blocking agents. While the data suggest that terazosin may provide some minor advantage in symptom relief over the other agents, and that there are some differences in the incidence of specific side effects, only a properly conducted double-blind comparative trial will reveal meaningful differences between agents'. In the statement from the publishers it stated that 'Author Dr Franklin Lowe, St Luke's – Roosevelt Hospital Centre, New York, concludes in the paper that 'there are no dramatic differences in the overall efficacy and safety of currently available alpha-blocking agents.' This conclusion is consistent with previous reviews and with the published findings of the 4th International Consultation on BPH.' This was certainly not the impression gained from page 3 of the detail aid.

Yamanouchi alleged that the information and comparison clearly misled (Clause 7.2), the artwork was neither fair nor balanced (Clause 7.6) and the overall impression was that tamsulosin was inferior, which, as there was no evidence to support this, was disparaging (Clause 8.1).

Yamanouchi noted that it had been in correspondence with Abbott previously over its use of non-comparable data. A copy of the correspondence was provided. The matter was never resolved; Yamanouchi had anticipated that by drawing Abbott's attention to the issue in its previous detail aid, it would take heed of the warning and would not repeat it. However, not only had Abbott disregarded Yamanouchi's earlier concerns, but the format in which it was now presenting the data was considerably more blatant.

RESPONSE

Abbott stated that the promotional item was used to promote Hytrin BPH to consultant urologists and their senior colleagues, and not to general practitioners. Yamanouchi claimed that the intended audience would be misled by the data presented on this piece and asserted that 'they neither have the time, nor always the specialist knowledge, to question (the data)'. Abbott disputed this and stated that the intended audience was experienced clinicians, well versed in available therapeutic options, existing therapeutic issues and data analysis.

Abbott accepted that, where available, promotional material should present published comparative data in preference to non-comparative data. To date, there had been no comparative, randomised controlled studies conducted which assessed the efficacies of UK licensed alpha-blockers, at UK licensed doses, for the treatment of BPH.

In a letter to Abbott, Yamanouchi had repeatedly drawn attention to the differences in methodologies between the various studies presented. Abbott accepted that these data resulted from non-comparative studies and this was clearly stated on the promotional item in question. However, with the current focus of the medical profession on the practice of evidence based medicine, and in the absence of such comparative data, Abbott believed that it was acceptable to present a review of available non-comparative data to allow appropriate prescribing decisions to be made by physicians, assuming that these were accurate, representative, and did not attempt to mislead.

The data on page 3 were taken from a fully peer reviewed abstract of a review of alpha-blockers for BPH (Lowe (1999)). Data presented in this manner had been accepted for publication in Prostate Cancer and Prostatic Diseases. Abbott acknowledged that the bar chart had been adapted from the original to remove reference to studies which had used non-UK licensed maintenance doses of alpha-blockers, and the text within the chart drew attention to this – 'Studies using licensed maintenance doses of alpha-blockers'.

Yamanouchi implied that the studies presented were fundamentally flawed and that no meaningful conclusions could be drawn from them. As these data had been independently reviewed by an eminent opinion leader in this therapeutic area, fully peer reviewed and accepted for publication, Abbott disputed this. The studies presented used licensed maintenance doses of Hytrin BPH and were of acceptable design and statistical analysis. The logical

extension of Yamanouchi's argument was that the current move towards presenting data in the form of a meta-analysis was wholly unacceptable. However, no two studies ever contained identical patient populations, were ever of identical design, or ever used identical methods of statistical data analysis. The argument proposed by Yamanouchi was therefore unrealistic.

Yamanouchi claimed that the data presented by Abbott was an 'unscientific review'. Abbott did not accept this. The issues raised by Yamanouchi were correct, but the interpretation of their significance was not. In response to the specific issues raised by Yamanouchi, Abbott stated:

a) Abbott accepted that different symptom scores were used to demonstrate efficacy in the studies presented. However, the range of symptom scores used applied equally to both Hytrin BPH and tamsulosin. In addition, it was the percentage improvement in symptom score over placebo that was being presented, not the absolute improvement. This was an acceptable method of presenting the data given that they arose from non-comparative studies.

b) Yamanouchi had highlighted that, as the symptom scores showed marked variation at entry into the various studies, the resulting data were meaningless. Abbott refuted this. The symptom scores included in Yamanouchi's table represented inclusion criteria, not average baseline symptom scores. Although the inclusion symptom scores for Lepor *et al* (1996) (terazosin) were given as AUA > 8, and Lepor (1998) (tamsulosin) as AUA > 13, the actual average baseline AUA scores for these studies were similar (16 and 19 respectively). In addition, the average baseline peak urinary flow rates were also very similar, most falling within the range of approximately 5-15mls. As flow rate improvements might be regarded as more acceptable indicators for efficacy, and the patients in these studies fell within a common range, there was actually very little difference between patient populations in this regard.

c) With regard to length of treatment, Yamanouchi again highlighted the differences between the studies presented. Abbott accepted that studies of differing duration were presented, however it was generally accepted in this therapeutic area that there was very little increase in response seen with this class of medicines beyond 12 weeks of therapy.

d) Yamanouchi highlighted the differences in placebo responses between the studies. Once again, this was accepted. However the assertion that this would undoubtedly bias the results was not. There was actually very little difference between the range of placebo responses for the terazosin and tamsulosin data (11-24% and 18-28% respectively).

In addition, there appeared to be little correlation between the degree of placebo response and ultimate clinical outcome for the terazosin group of data, as was suggested by Yamanouchi. Abbott referred to a table it had produced which compared the placebo response (% symptom score) and the symptom score over placebo of four of the seven studies featured in the bar chart.

Abbott noted that the Code did not prohibit the use of non-comparative data, but acknowledged presentation of comparative data in this promotional piece would be preferable to presenting data from non-comparative studies. However, in the absence of such data, Abbott believed that it had presented the available data fairly, accurately, and with no intention to mislead. The following points confirmed Abbott's commitment to ensure that this was the case.

The text did not refer to any claim of superiority for Hytrin BPH. The reader was clearly informed, in bold text and in a large font size, that the presented data represented 'attributable improvements above placebo in separate, non-comparative studies'. These studies were then appropriately referenced. Furthermore, this point was reiterated below the bar chart on this page ('How the 'selective' alpha-blockers compare in published randomised placebo-controlled double-blind clinical studies'). Thus the reader was clearly informed that the data arose from non-comparative studies.

The bar chart had been specifically designed so as not to mislead or misinform, and in particular to emphasise that the studies were non-comparative. The name of the lead author, the sample size, year of publication, full reference and the dose of the medicine used in each study were clearly stated.

With regard to the overall visual appearance of the data, Abbott disputed that there was any misrepresentation. No claim of superiority for Hytrin BPH was inferred. The data had not been manipulated. They were accurate and representative of the available published data, and were presented in a manner which was available in the public domain. Abbott therefore denied breaches of Clauses 7.2, 7.6 and 8.1 of the Code.

PANEL RULING

The Panel noted that the data was derived from separate non-comparative studies and considered that such data might be acceptable in certain circumstances; relevant factors would include the therapy area, the intended audience, how the data was presented and the conclusions drawn. In this regard the Panel noted that the intended audience comprised consultant urologists and their senior colleagues.

The Panel noted that the data were taken from a literature review of alpha-blockers for BPH (Lowe (1999)) which was provided to the Panel in the form of a press release dated 7 April 1999 which reproduced the text of the abstract together with a key figure and stated that it had been accepted for publication. The review sought to evaluate the pharmacological and physiological selectivity as well as the clinical efficacy and safety of alfuzosin, doxazosin, tamsulosin and terazosin in the treatment of BPH. The abstract featured the original bar chart, which had been adapted in the detail aid to exclude studies with non-UK licensed maintenance doses of alfuzosin and tamsulosin. The author concluded that there were 'no dramatic differences in the overall efficacy and safety of currently available alpha-blocking agents. While the data suggests that

terazosin may provide some minor advantage in symptom relief over the other agents … only a properly conducted, double-blind, comparative trial will reveal meaningful differences between agents.' The accompanying Stockton Press Release stated that the author's conclusions in this regard were consistent with previous reviews and the published findings of the 4th International Consultation on BPH.

The Panel noted the differences in methodology between the 12 studies at issue. Different symptom scores had been used, IPSS, AUA symptom score, Boyarsky symptom score and modified Boyarsky. Elhilali *et al* (1996) had used both Boyarsky and AUA whilst Buzelin *et al* (1997) had used IPSS and Boyarsky's derived score. The Panel did not accept that one could make valid comparisons with different symptom scores. The Panel noted that the authors of Chapple *et al* (1996), itself a meta-analysis of two separate placebo controlled studies which compared the efficacy and safety of modified release tamsulosin, noted that comparisons of the results obtained for tamsulosin with results from other trials evaluating other alpha-blockers was difficult owing to differences in patient baseline characteristics, inclusion criteria and methods for evaluating efficacy. Further it was noted that there was a pronounced and well documented placebo effect in patients with symptomatic BPH.

The Panel noted Abbott's submission that baseline symptom scores at entry were similar but did not accept that it was appropriate to assume, in the absence of evidence, that response at 12 weeks would be similar to response at 52 weeks. Whilst the Panel noted Abbott's submission that the range of placebo response was similar for all products and did not correlate with clinical outcome, the Panel noted that the table produced by Abbott showed that the lowest placebo response was associated with the highest percentage symptom score over placebo.

The Panel noted that whilst the studies were clearly stated to be non-comparative, the heading referred to setting standards and the text beneath the bar chart stated 'How the selective alpha-blockers compare in published randomised placebo-controlled double-blind clinical studies'. The Panel considered that the page invited the reader to directly compare data from non-comparative studies and implied that it was appropriate to do so. In the opinion of the Panel there was no valid basis for comparison of these studies in this way. Further the page gave the impression that Hytrin BPH was superior to other agents, which, given the conclusions of Lowe (1999), was not so. The Panel considered the page misleading as alleged and ruled a breach of Clause 7.2 of the Code.

The Panel noted that Clause 7.6 stated *inter alia* that graphs and tables must be presented in such a way as to give a clear, fair, balanced view of the matters with which they deal. The supplementary information to Clause 7.6 stated that care must be taken to ensure that artwork did not mislead as to, *inter alia*, any claim or comparison. 'It should also be noted that if a table, graph etc in a paper is unacceptable in terms of the requirements of the Code because, for example, it gives a visually misleading impression as to the data shown, then it must not be used or reproduced in promotional material.'

The Panel noted that the data for Hytrin BPH, tamsulosin and alfuzosin showed a range of symptom score improvements over placebo of approximately 9-31%, 9-14% and 13% respectively. Five of the seven bars representing the data for Hytrin BPH each represented a greater percentage symptom score improvement than each bar representing data for tamsulosin and alfuzosin. The Panel noted the conclusions of Lowe (1999). The Panel considered that the bar chart gave the impression that Hytrin BPH was more effective than the other products and thus gave a visually misleading impression of the differences between the products. A breach of Clause 7.6 was ruled. The Panel ruled a breach of Clause 8.1 as alleged.

A2 Terazosin studies

COMPLAINT

Yamanouchi alleged that the titration doses used in the terazosin studies were not in accordance with the SPC. The SPC stated that 'Treatment should be initiated using the Hytrin BPH Starter Pack and response to treatment reviewed at four weeks.' The titration schedule in the pack was 7 days x 1mg, 14 days x 2mg and 7 days x 5mg. In fact, the 'strict compliance' stipulated in the SPC in order to minimise acute first-dose hypotension by starting with the 1mg dose, could only be met through the starter pack as 1mg tablets were only available as part of the starter pack. As shown in a table provided by Yamanouchi, the titration rates in the studies quoted were considerably more rapid, or slower, each having the potential to affect efficacy results, both on an 'intent-to-treat analysis,' or on a 'per protocol analysis.'

Abbott's response to Yamanouchi's concern regarding dosing schedule was that 'it is the maintenance dose that is of relevance.' This, however, was an over-simplistic view and not correct. The reason that it was not correct and that the rate of titration was relevant was that different titration schedules would affect both side effects and improvement in symptoms. Each of these in turn would affect patients' agreement to remain in the study. With either a too rapid or too slow titration regime, compared with the standard, different patients would drop out of the study at different time points for different reasons. Therefore, the population remaining in the study at the end would be different in the three situations. From the data available there was no way of knowing how the different titration rates affected the population which chose to withdraw or remain in the study. Consequently, as each titration schedule created a different population at the end of the study, then the efficacy results, regardless of length of study or equivalent maintenance doses, could not be extrapolated to be that result that would be obtained with the SPC schedule.

For example, a too rapid schedule was likely to cause more patients to drop out early because of intolerance, too slow a regime might cause different patients to withdraw from the study as they did not notice sufficient benefit soon enough. Either way, both

patient numbers and patient characteristics would be different in each scenario at the end of the study, due to the different biases resulting from the different dosing schedules used. A comparison of patients randomised compared with the number of patients analysed quoted in the detail aid was provided by Yamanouchi in a table.

Yamanouchi stated that if, for example, the SPC titration had been used in the Lepor (1992) study, at the 10mg dose, the 54 (77%) of patients whose data had contributed to this efficacy analysis would have been different patients – and therefore with different efficacy results as inevitably different patients responded differently to the same medication and could give a (very) different mean score. There was no way of knowing how similar or different the result would have been.

Abbott was using these studies to promote the efficacy of terazosin, and as the titration schedule over the first few weeks of the studies was not in accordance with that which clinicians would be expected to use according to the SPC (and might consequently affect the efficacy results), this was promotion of efficacy studies which were inconsistent with the particulars listed in the SPC (Clause 3).

It was also misleading as the doctor would assume that the data were applicable to his patients and was therefore in breach of Clause 7.2.

RESPONSE

Abbott stated that all studies in the marketing authorization application for Hytrin BPH used titration to response/fixed dose titration regimens which differed to that referred to in section 4.2 of the Hytrin SPC. The current starter pack was practically designed to ensure that the patient received the most efficacious dose in a safe manner.

Section 4.2 of the Hytrin BPH SPC referred to a 'guide to titration', and stated that 'the dose of terazosin should be adjusted according to the patient's response'. It did not dictate that there was only one method of recommended dose titration, and warn against deviating from this recommendation. As such, it allowed for a degree of prescriber flexibility, based on clinical judgement, as to when it was appropriate to amend the dose.

Abbott reiterated that, in terms of efficacy, it was the maintenance dose which was important, as the titration phase was not a major contributor to efficacy. As had been previously stated, Abbott had clearly acknowledged to the reader that the presented data arose from non-comparative studies.

All of the dosages of terazosin used in these studies, 1mg, 2mg, 5mg and 10mg, were licensed doses for the treatment of BPH, which included initial dose titration. These were listed under section 2 of the Hytrin BPH SPC. The titration regimens referred to in the terazosin studies were therefore not inconsistent with the Hytrin BPH SPC. Abbott therefore denied a breach of Clause 3.

In its letter of complaint, Yamanouchi had presented a table to emphasise its point that the number of patients included in the efficacy analysis influenced ultimate efficacy outcomes. Once again, Abbott accepted this point in general. However, the percentage of patients included in the efficacy analyses for the terazosin studies was actually perfectly acceptable (ranging from 77 to 100%). For example, it was highly unlikely that the efficacy results obtained for the Roehrborn (1996) study would be very much different if 100% of patients had been included in the efficacy analysis, as opposed to the 93% that actually were. Abbott did not accept that the value of the efficacy data arising from these studies was therefore flawed.

In addition, as the use of non-comparative data had been clearly stated, and the doses used for titration in these studies were consistent with the marketing authorization for Hytrin BPH, Abbott did not accept that presentation of these data constituted a breach of Clause 7.2.

PANEL RULING

The Panel noted that section 4.2 of the Hytrin BPH SPC, headed 'Posology and Method of Administration' stated that 'The dose of terazosin should be adjusted according to the patient's response. The following is a guide to administration: Initial dose 1mg before bedtime is the starting dose for all patients and should not be exceeded. Strict compliance with this recommendation should be observed to minimise acute first-dose hypotensive episodes. Subsequent dose. The dose may be increased by approximately doubling at weekly or bi-weekly intervals to achieve the desired reduction in symptoms. The maintenance dose is usually 5 to 10mg once daily.' It was also stated that treatment should be initiated using the Hytrin BPH Starter Pack and response reviewed at four weeks.

The Panel noted that whilst the titration schedule in the starter pack was 7 days x 1mg, 14 days x 2mg and 7 days x 5mg the SPC only required strict compliance with the starting dose of 1mg, the requirements in relation to subsequent dosing were less precise and could be tailored to individual patient response. The Panel noted that in each of the Hytrin BPH studies referred to in the bar chart a starting dose of 1mg was used, thereafter the dose was titrated at varying rates. Whilst the titration rates at issue were different to the starter pack the Panel did not consider them to be inconsistent with the SPC and ruled no breach of Clause 3.2 of the Code.

The Panel accepted that the titration regimen could affect the number of dropouts and consequently the patient population. The Panel noted Abbott's acceptance of the general point that the number of patients included in the efficacy analysis influenced ultimate efficacy outcomes. It could not therefore be assumed that efficacy with one titration regimen was relevant to efficacy with another. The Panel noted that the titration rates differed markedly. The Panel considered that its general comments about the differences between the studies at A1 were relevant here. It was likely that doctors would use the starter pack for most patients and the efficacy results presented were not necessarily relevant to these

patients. The Panel considered that the use of the efficacy data without further explanation was misleading and ruled a breach of Clause 7.2 of the Code.

B Page 7 headed 'Nocturia: Have a good night with Hytrin BPH'

This page bore a bar chart which showed the percentage improvement in nocturia seen in separate published studies with a bar each for Hytrin BPH (43%), tamsulosin (29%), alfuzosin (18%) and indoramin (19%). Each bar was labelled with the percentage improvement, the patient numbers and each was referenced to a separate study. A sub-heading to the page stated 'Hytrin BPH: Published improvements in nocturia' with a reference to a small footnote to the claim at the bottom of the page which stated 'non-comparative data'. The sub-heading was referenced to four separate studies.

B1 The comparison

COMPLAINT

Yamanouchi alleged that the bar chart was designed to mislead the reader into believing that Hytrin BPH had a much more significant effect on nocturia than tamsulosin, alfuzosin and indoramin, when there was no evidence to support this claim.

The results of the trials depicted on the bar chart for nocturia could not be compared, as once again the trial methodologies and duration were vastly different, as shown clearly in a table which Yamanouchi provided.

Yamanouchi stated that following a lead-in period, the Debruyne *et al* (1996) Hytrin BPH study commenced with a 26 week single-blind phase, during which all patients were titrated up to 10mg terazosin daily, which was reduced to 5mg daily in those patients who could not tolerate the higher dose. There was no comparator group during this single-blind period. After 26 weeks, patients who had responded to terazosin treatment were then randomly assigned to continue with their dose of terazosin or receive placebo for a 24 week 'withdrawal period'. During the single-blind period, terazosin did indeed produce a 42.9% improvement in nocturia from baseline to the final visit as illustrated on the bar chart. However, during the subsequent double-blind 'withdrawal' period, nocturia worsened in both the terazosin and the placebo groups, such that there was no significant difference in nocturia between the two groups at week 50 of the whole study (week 24 of the second phase of the study).

In contrast, the three comparator trials depicted in the bar chart were short-term double-blind trials of half to an eighth of the duration of even just the single-blind phase of the terazosin study.

Furthermore, the methodologies of the statistical analyses used in the studies were not comparable. There was no intention-to-treat (ITT) analysis in the Debruyne study. 378 patients began the single-blind phase of this study, but only 273 (72.2%) were evaluable at the end. It was these 72.2% of patients who showed a mean improvement in nocturia score of 42.9%. The other 105 patients were lost to follow up or withdrew due to adverse events during this single-blind phase. Therefore, the 42.9% improvement in nocturia score related only to a subset of the original study population – those who were able to tolerate terazosin and remained in the first part of the study for the full 26 weeks. In contrast, in the comparator tamsulosin study Abrams *et al* (1995), the results were analysed on an ITT basis. After the two week run-in period 296 patients entered and 276 patients completed the double-blind phase, and results from 289 patients were used in the analysis of efficacy (including nocturia) – patients who dropped out of the study for whatever reason were still included in the analysis (provided there was at least one efficacy recording during the double-blind phase).

As with the visual at A1, the doctor relied on the integrity of the industry for comparisons, if they were to be made, to be fair.

The information and comparison on this page clearly misled (Clause 7.2), the artwork was neither fair nor balanced (Clause 7.6) and the overall impression was that tamsulosin was inferior, which, as there was no evidence to support this, was disparaging (Clause 8.1).

RESPONSE

Abbott stated that the text on this page made no claim of superiority for Hytrin BPH over the other alpha-blockers mentioned.

As nocturia was often perceived by BPH sufferers as one of the most troublesome symptoms Abbott believed that it was acceptable to present a review of the available data, as long as this was accurate, representative, and did not intend to mislead. Once again, the reader was informed that these data represented 'published improvements' in nocturia, and was reminded, that the data arose from non-comparative studies.

With regard to the graphical representation of the data, Abbott had taken the following steps to highlight that the data arose from non-comparative data: inclusion of the name of the lead author, an appropriate reference, details of the sample size, and reiteration that the data arose from 'separate published studies'.

With regard to the overall visual appearance of the data, Abbott denied that there had been any misrepresentation in order to deceive the reader and infer a claim of superiority for Hytrin BPH. The data had not been manipulated. They were accurate and representative of the available published data.

The complaint drew particular reference to the 42.9% improvement in nocturia score presented for Hytrin BPH, and referenced to Debruyne (1996). Yamanouchi claimed that this degree of improvement applied only to those patients who completed the single-blind period, and that there was no significant difference in nocturia scores between patients receiving terazosin or placebo by the end of the double-blind period.

Abbott stated that this was correct, however Yamanouchi had misinterpreted the significance of this result. At the end of the single-blind period, all patients who received terazosin (and completed this phase of the study) had improved their nocturia score from a mean baseline of 2.4 to 1.4 (a mean 42.9% improvement). Sub-analysis of those who were subsequently entered into the double-blind period (ie the 'responders') demonstrated that this group had improved their mean nocturia score from 2.6 to 1.3 (ie a 50.6% increase), by the end of the single-blind period. This study was designed to enter all patients who had responded to terazosin (responders) into a further double-blind period, where patients were randomised to either continue with terazosin, or switch to placebo. This was entirely appropriate, and was an acceptable form of study design.

At the end of the double-blind period, there was no significant difference in nocturia scores between terazosin or placebo recipients. This did not mean that no effect on nocturia was seen overall. These data demonstrated that once significant improvement was made in nocturia scores in the early stages of terazosin therapy (ie as shown by the results at week 26), further improvements were unlikely. This effect was predictable, given the pharmacological effects (ie relaxation) brought about by terazosin on the bladder neck and detrusor muscle in obstructed uropathy states.

Although this study attracted criticism from Yamanouchi, the author, an extremely well respected experienced clinical trialist, concluded that 'treatment with terazosin has a beneficial effect on BPH, continuing for at least 12 months, and can be safely considered for medium to long-term use in those who benefit'.

Consequently, Abbott did not accept that the data on this page were misleading or presented unfairly. They were the only available published, peer reviewed data, that specifically reported on improvements in nocturia score for the alpha-blockers listed. Breaches of Clauses 7.2, 7.6 and 8.1 were denied.

PANEL RULING

The Panel considered that its ruling at A1 above was relevant. Data from separate non-comparative studies had been presented. The study from which each set of data was derived was clearly stated. In the opinion of the Panel the bar chart would invite the reader to compare the percentage improvement in nocturia for each medicine. The Panel considered that the methodology of the studies differed markedly in terms of duration of treatment and statistical analysis such that the comparison was unfair. The Panel considered the bar chart misleading as alleged and ruled breaches of Clauses 7.2 and 7.6 of the Code. The Panel ruled a breach of Clause 8.1 as alleged.

B2 Debruyne *et al* (1996) terazosin study

COMPLAINT

Yamanouchi stated that a similar situation applied here as for page 3 of the detail aid. The titration schedule followed in the single-blind phase of the Debruyne terazosin study (1 x 1mg; 13 x 2mg; 28 x 5mg; 28 x 10mg) was more rapid than that specified in the SPC. Once again, this was promotion of efficacy, the data for which had been derived from a study which used a titration schedule which was inconsistent with the SPC. In this study, 427 patients were enrolled in the single-blind part of the study; 378 were considered 'evaluable,' and of those, 273 completed the single-blind period. The analysis was undertaken on those 273 patients (ie on only 64% of the patients who entered the study). 105 of the 'evaluable' patients were lost to follow-up or withdrew for adverse events (ie 38% of the evaluable patients). With a more rapid titration schedule than allowed under the SPC, it was perhaps not surprising that there was a high drop-out of patients. But a claim for efficacy based on a self-selected group of patients (ie on those able or prepared to tolerate a rapid titration schedule) was not necessarily representative of the efficacy results which would have been obtained if all 378 (or even the 273) patients had been given the recommended titration schedule. Both different numbers and different patients would have dropped out in the latter situation. There was therefore no way of knowing the validity of the efficacy claim when applied to patients treated according to the SPC. Yamanouchi alleged that the use of results to promote a medicine which was derived from data which was inconsistent with the particulars listed in the SPC was in breach of Clause 3.

It was also misleading as doctors would assume that the data were applicable to their patients and therefore in breach of Clause 7.2.

RESPONSE

Abbott reiterated that the dosages of terazosin used in the study were all licensed doses for the treatment of BPH, and consistent with the marketing authorization for Hytrin BPH. Abbott did not accept that presentation of these data constituted a breach of Clause 3.

Given that Abbott believed the dosing regimen used in this study was consistent with the SPC, it disputed that the results of the study were of no relevance to patients treated according to the SPC. Abbott therefore also denied a breach of Clause 7.2.

PANEL RULING

The Panel considered that its ruling at A2 was relevant here with regard to the differences between the titration regimen applied in Debruyne *et al*, the titration regimen recommended by the SPC and that provided for in the starter pack. The Panel thus ruled a breach of Clause 7.2 and no breach of Clause 3.2 of the Code.

C Page 9 headed 'Hytrin BPH: Tailoring treatment for individual patient management'

Beneath the sub-heading 'Treatment is not restricted by a single, licensed dosage regime,' a bar chart compared the efficacy of Hytrin BPH 5mg and 10mg; results showed that 67% and 79% of patients

respectively obtained ≥ 30% symptom improvement. Beneath the bar chart two claims appeared; 'With Hytrin BPH it is possible to increase the dose to achieve greater symptom control' and 'Tailoring of dose allows more patients to achieve significant relief.' Both claims and the bar chart were referenced to data on file, Abbott Laboratories, Study M87-012.

C1 The comparison

COMPLAINT

Yamanouchi stated that it did not consider that Abbott's data on file supported the apparent hanging comparison 'Tailoring of dose allows more patients to achieve significant relief.' Yamanouchi presumed that this statement was intended to mean that more patients achieved significant relief than if the dose was not tailored. However, as there was no group whose dose was not tailored in the study cited, Yamanouchi did not understand how the reference could support this claim. It was not known whether patients would have achieved the same 79% or greater improvement if all patients had been given 10mg at the outset, ie it was not proven that it was the tailoring of the dose that allowed more patients to achieve relief, as opposed to the same or better result being achieved by giving a sufficiently high dose for maximum effect at the outset and was therefore in breach of Clause 7.4.

The study itself was a double-blind study and without the placebo group results, a p-value or patient numbers, it was impossible to judge the clinical benefit of the responses in the terazosin group and, as such, was therefore not a clear, fair or balanced presentation of the data and was in breach of Clause 7.6.

The data on file sent by Abbott in response to Yamanouchi's request had not elucidated the claims and was therefore in breach of Clause 7.3.

RESPONSE

Abbott stated that in inter-company correspondence Yamanouchi had requested clarification of the statement 'Tailoring of dose allows more patients to achieve significant relief'. Abbott responded appropriately with a detailed explanation of the intended message, as supported by the relevant reference.

As Yamanouchi had identified, patients responded differently to the same medicine. Therefore, the clinically effective dose of Hytrin BPH was patient specific. The dose of terazosin should be tailored according to the patient's response. Some patients would receive adequate symptom relief at a dose of 2mg; others might require higher doses to achieve similar benefit. A patient who had only responded minimally, for example, to 2mg of terazosin, might respond to a greater degree, for example, to 5mg.

This page was designed to highlight this dosing flexibility as an advantage for terazosin, ie that 'treatment is not restricted by a single, licensed dosing regime', and that 'tailoring of the dose allows more patients to achieve significant relief (from symptoms)'. In this context, dose tailoring referred to flexibility of dose. In addition, there was no 'hanging comparison', as the reference was quite clearly to other doses of terazosin.

Abbott considered that the data on this page were clearly presented: 67% of patients who received 5mg of terazosin in the quoted study achieved ≥ 30% of symptom improvement. Of those who had not responded to this dose of terazosin, and who were able to tolerate the increased dose, a further 12% of patients experienced clinical benefit (cumulative percentage of 79%).

The abstract that Yamanouchi was provided with outlined the relevant study design and results pertinent to the data presented on the promotional item. No additional clarification was sought by Yamanouchi, and thus Abbott, not unreasonably, assumed that the clarification it had provided was acceptable.

The abstract supplied presented a sub-analysis of the main study. Doses of terazosin were increased according to clinical response and tolerability. It demonstrated that, of the 96 patients who received terazosin, 87 received 1-2mg of terazosin (9 excluded from analysis). Of these, 36 achieved a satisfactory clinical response, a percentage response rate of 41%. Of the 51 remaining patients, 8 were lost to efficacy analysis, leaving 43 patients who received terazosin 5mg. Of these patients, 19 had a clinical response, producing a cumulative response rate of 67%. Of the 24 patients remaining, 23 received terazosin 10mg (one excluded from analysis). Eight patients responded, producing a cumulative response rate of 79%. Of the remaining 15 patients, 6 were lost to analysis, thus 9 patients received terazosin 20mg. Of these, 2 responded and 7 did not. The cumulative response after the dose was tailored according to clinical response was therefore 85%.

Thus this study supported the clinical observation that increasing the dose of terazosin for certain patients might result in additional symptomatic improvement. In this study, an additional 12% of such patients experienced benefit through dose escalation (or dose tailoring).

There had been no clinician initiated issues raised about this page to date, nor had the sales force reported any clinician objections to the presentation or content of the data.

Abbott denied breaches of Clauses 7.3, 7.4 and 7.6 of the Code.

PANEL RULING

The Panel noted that Study M87-012 was a multi-centre placebo-controlled randomised dose titration study of once a day administration of terazosin in the treatment of the symptoms of BPH of 177 evaluable patients. The patients in the study had daily doses titrated upwards from 1mg to a maintenance dose of 2, 5, 10 or 20mg according to therapeutic response. The percentage of patients responding at or prior to each dose level was provided. The cumulative percentage response was calculated using the Kaplan-

Meier statistical method. The Panel noted Abbott's submission that the abstract presented a sub-analysis of the main study. No placebo results were provided and no p-values stated. Thus it was not known whether the difference in the percentage of patients with a ≥ 30% symptom improvement on Hytrin 5mg or 10mg was statistically significant nor whether these results were significant against placebo. The Panel considered that in the absence of this information it was thus not possible to judge the clinical significance of the data.

The Panel considered that the bar chart gave the impression that there was an important difference in the percentage of patients with ≥ 30% symptom improvement obtained at 10mg and 5mg Hytrin BPH and that this difference was of statistical significance. The bar chart thus gave a visually misleading impression of the data and a breach of Clause 7.6 of the Code was ruled.

The Panel considered that neither the statement 'Tailoring of dose allows more patients to achieve significant relief' nor the bar chart were substantiated by Study M87-012 as it was not possible to determine the significance of the results obtained. A breach of Clause 7.3 was ruled.

The Panel did not consider the phrase to be a hanging comparison, as alleged, and no breach of Clause 7.2 was ruled. It did not accept Yamanouchi's view that as no patient received 10mg from the outset it was not proven that the greater efficacy was due to the tailoring of dose, rather than simply to a higher dose. The Panel considered that the reader would reasonably assume tailoring to mean prescribing the most appropriate dose for the patient depending on therapeutic response. The Panel noted however that Yamanouchi had alleged a breach of Clause 7.4 in this regard.

The Panel noted that Clause 7.4 required substantiation to be provided without delay at the request of members of the health professions. The Panel noted that in response to the request for substantiation Abbott had provided Study M87-012. The Panel noted that it had ruled a breach of Clause 7.3 in that the study had not substantiated the statement and bar chart. Abbott had not, therefore, provided substantiation as required by Clause 7.4 and a breach of that clause was ruled.

C2 Titration schedule

COMPLAINT

Yamanouchi alleged that yet again the titration schedule followed in the Abbott data cited (3 x 1mg, titrated to final maintenance dose of 2, 5 and 10mg daily at unspecified intervals) was not that recommended in the Hytrin BPH SPC and could not be extrapolated for the same reasons as explained at point A2. Yamanouchi pointed out that the 20mg dose was not used in the detail aid. This again was promotion of an efficacy study based on data derived from the use of a titration schedule which was inconsistent with the particulars listed in the SPC, and consequently was in breach of Clause 3.

It was also misleading as doctors would assume that the data were applicable to their patients and therefore in breach of Clause 7.2.

RESPONSE

Abbott denied breaches of Clauses 3 and 7.2 and referred to its comments in relation to A2 above.

PANEL RULING

The Panel considered that its rulings at A2 and B2 were relevant and thus ruled no breach of Clause 3.2 and a breach of Clause 7.2 of the Code.

D Page 15 headed 'No clinically significant effect on blood pressure in normotensive and controlled hypertensive patients'

Beneath a sub-heading 'Hytrin BPH '… produced no clinically significant mean blood pressure changes in patients with a normal baseline DBP', this page bore a chart showing the effects of Hytrin BPH on diastolic blood pressure (DBP) in normotensive and controlled hypertensives with BPH.

Page 15 of the detail aid provided by Abbott differed from that provided by Yamanouchi in that immediately beneath the chart a sticker had been placed which stated 'When adding terazosin to a diuretic or other anti-hypertensive agent, dosage reduction and retitration may be needed. Please refer to Summary of Product Characteristics before initiating therapy.' The allegations at D1, D2 and D3 were considered in relation to the material complained of and provided by Yamanouchi.

D1 Alleged breach of Clause 3

COMPLAINT

Yamanouchi alleged that this page (the heading in particular, but also the sub-heading and the chart), was misrepresentative in two serious respects. Firstly, the reader was led to believe that Hytrin BPH could be prescribed without risk of hypotension to a treated hypertensive patient without any specific caution or dose adjustment. This was contrary to the Hytrin BPH SPC which stated:

'Caution should be observed when terazosin is administered with other antihypertensive agents to avoid the possibility of significant hypotension. When adding terazosin to a diuretic or other anti-hypertensive agent, dosage reduction and retitration may be needed.'

The information presented on this page could influence, in fact encourage, prescribers to act against the advice in the SPC, putting the treated hypertensive patient at risk.

Secondly, in view of the extensive SPC wording on postural hypotension, Yamanouchi was really quite amazed that Abbott could made the statement that its product had 'No clinically significant effect on blood pressure in normotensive … patients'. Yamanouchi considered postural hypotension to be a clinically significant result of an effect on blood pressure.

The relevant sections of the SPC that drew attention to the problems of postural hypotension in potentially normotensive patients were:

'Initial dose: 1mg before bedtime is the starting dose for all patients and should not be exceeded. Strict compliance with this recommendation should be observed to minimise acute first-dose hypotensive episodes.

Postural hypotension: postural hypotension has been reported to occur in patients receiving terazosin for the symptomatic treatment of urinary obstruction caused by BPH. In these cases, the incidence of postural hypotensive events was greater in patients aged 65 years and over (5.6%) than those aged less than 65 years (2.6%).

Special warnings and precautions: In clinical trials, the incidence of postural hypotension was greater in patients who received terazosin for BPH than in patients who received terazosin for hypertension. In this indication the incidence of postural hypotensive events was greater in patients aged 65 years or over (5.6%) than those aged less than 65 years (2.6%). *(Yamanouchi comment: many of these patients will have been normotensive.)*

Effects on ability to drive and use machines: Dizziness, light-headedness or drowsiness may occur with the initial dose or in association with missed doses and subsequent reinitiation of Hytrin therapy. Patients should be cautioned about these possible adverse events and the circumstances in which they may occur and advised to avoid driving or hazardous tasks for approximately the first 12 hours after the initial dose or when the dose is increased.

Undesirable effects: Hytrin, in common with other alpha-adrenoceptor antagonists, may cause syncope. Syncopal episodes have occurred within 30 to 90 minutes of the initial dose of the drug. Syncope has occasionally occurred in associated with rapid dosage increases or the introduction of another antihypertensive agent. In clinical studies in hypertension, the incidence of syncopal episodes was approximately one per cent … Dizziness, light-headedness or fainting may occur when standing up quickly from a lying or sitting position.'

Yamanouchi did not consider that Abbott's proposal in inter-company correspondence of a sticker with a rider was in any way sufficient to counter the extremely bold headline.

This page, and the header in particular, were not in accordance with the particulars listed in the SPC and were therefore in breach of Clause 3 of the Code.

RESPONSE

Abbott denied that the text and data presented on this page represented a serious safety issue.

Terazosin was licensed both as Hytrin BPH, for the treatment of benign prostatic hyperplasia, and as Hytrin, for the treatment of hypertension. Terazosin was not a new medicine. The detail aid was used to promote Hytrin BPH to consultant urologists, and their senior colleagues. These were experienced clinicians, well versed in available therapeutic options and existing therapeutic issues. The effect of Hytrin BPH on blood pressure, in normotensives, hypertensives and controlled hypertensives was a question frequently asked of the sales force. BPH and hypertension commonly co-existed in patients.

The heading on the page was factual, scientifically accurate and fully substantiated by the accompanying references. The references supported that minimal reductions in blood pressure were observed when terazosin was administered to normotensive patients, and those with hypertension controlled by concomitant anti-hypertensive therapy. Additional data supported the conclusions from these studies (Kirby (1998), Brawer (1993)).

The attention of the prescriber was clearly drawn to the location of the prescribing information for Hytrin BPH. This cautioned the prescriber about concomitant anti-hypertensive use, therapy modification and adverse effects, including postural hypotensive effects. This was a fundamental aspect of medical practice, and Abbott refuted the allegation that it was encouraging prescribers to do otherwise.

Abbott denied a breach of Clause 3.

PANEL RULING

The Panel noted that Section 4.5 of the SPC headed 'Interactions' advised caution when administering Hytrin BPH with other anti-hypertensive agents to avoid the possibility of significant hypotension. The Panel further noted the references in the SPC to the problems of postural hypotension as stated by Yamanouchi. The Panel noted that terazosin was licensed as Hytrin for the treatment of hypertension. Terazosin was therefore likely to have an effect upon blood pressure. The Panel considered that the page gave the impression that Hytrin BPH treatment was not associated with an effect on blood pressure in normotensive or controlled hypertensive patients which was not so and inconsistent with the Hytrin BPH SPC. A breach of Clause 3.2 was ruled.

D2 Claim Hytrin BPH '…produced no clinically significant mean blood pressure changes in patients with a normal baseline DBP'. The claim was referenced to Debruyne *et al* (1996).

COMPLAINT

Yamanouchi stated that whilst the quotation was taken directly from the Debruyne paper, to use a quotation from a paper with very unusual methodology to imply a safety and adverse event profile which ran so contrary to the many warnings in the SPC was highly inappropriate and did not reflect available evidence (assuming the SPC could be taken to be 'available evidence,' ie, '… the incidence of postural hypotensive events was greater in patients aged 65 years and over (5.6%) than those aged less than 65 years (2.6%)'). A breach of Clause 7.7 was alleged.

RESPONSE

Abbott denied that the Debruyne paper did not reflect available evidence. Data were submitted that

demonstrated that the results obtained in this study were similar to those of other researchers (Kirby (1998); Brawer (1993) and Lowe (1994)). The data presented on this page detailed the effects of terazosin on blood pressure in normotensive and controlled hypertensives. There was no attempt to minimise the safety issues surrounding administration of terazosin to patients receiving anti-hypertensives. On the contrary, the attention of the prescriber was clearly drawn to this.

Abbott denied a breach of Clause 7.7.

PANEL RULING

The Panel noted that Clause 7.7 stated that information and claims about side-effects must reflect available evidence or be capable of substantiation by clinical experience.

The Panel noted its ruling at B2 and A2 with regard to Debruyne *et al* (1996). The Panel noted that the quotation at issue was an accurate reflection of the findings of Debruyne with regard to mean blood pressure which was not affected in a clinically significant way. The Panel considered that its ruling at D1 was relevant with regard to statements in the SPC regarding postural hypotension in some patients and the overall impression of the page. The Panel considered that the quotation in this context underlined the general impression that Hytrin BPH was free from problems with blood pressure changes which was not so. A breach of Clause 7.7 was ruled.

D3 Chart referenced to Lowe (1994)

COMPLAINT

Yamanouchi stated that the Lowe study was a combined analysis of 6 placebo controlled studies.

At least one of these studies used a titration dose which was excessively slow compared to the UK dosage recommendations, being 1mg daily for four weeks, then increasing the dose every four weeks to 10mg, ie taking three months to reach the first 10mg dose (one month at each of 1mg, 2mg and 5mg) compared with the SPC where the 10mg dose could be introduced after one month. Even for the 5mg dose, this was not reached in this study until after 8 weeks, compared with the Hytrin BPH Starter Pack, where it was introduced at week 3. The SPC advised that transient side effects might occur at each titration step and it was inevitable that hypotension would be minimised with such a considerably slower titration schedule. This would therefore bias the results towards a more favourable side effect profile than would be seen using the SPC mandated starter pack.

The safety data used to support this chart was derived from studies, certain of which were inconsistent with the particulars of the SPC at least one of which would give an unfairly favourable result with regard to the problems of hypotension. This was in breach of Clause 3.

The impression gained from the chart was that there were no problems with hypotension. This sat very uncomfortably with the considerable references in the SPC to the problems of postural hypotension (see D1 above). The chart gave a false impression of the side effect profile that would be anticipated and indicated in the SPC and, as such, was misleading (breach of Clause 7.2), nor were the specifics of the data capable of substantiation from data that accorded with the particulars of the SPC (breach of Clause 7.7).

Additionally, no patient numbers were quoted on the chart. In fact, whilst the combined analysis had 519 + 293 normotensive patients, there were only 18 controlled hypertensive patients on terazosin and 12 on placebo, so it was not surprising with such a small sample that p = NS. The chart therefore was meaningless and consequently misleading (breach of Clause 7.2) and did not give a balanced view of the matter (breach of Clause 7.6).

RESPONSE

Abbott pointed out that the dosages of terazosin used in these studies were all licensed doses for the treatment of BPH, which included initial dose titration. These were listed under Section 2 of the Hytrin BPH SPC. Only one of the studies in the Lowe paper allowed a 20mg dose. Although the Hytrin BPH SPC stated that there were insufficient data to suggest additional symptomatic relief with doses above 10mg, it did not prohibit this dose (the dose of terazosin should be adjusted according to the patient's response).

The Hytrin BPH SPC provided guidance to the prescriber as to how to initiate therapy. It did not dictate that there was only one method of recommended dose titration, and warn against deviating from this recommendation. As such, it allowed for a degree of prescriber freedom, based on clinical judgement, as to when it was appropriate to amend the dose. The titration regimens referred to in the Lowe paper were thus consistent with the Hytrin BPH SPC. Abbott therefore denied a breach of Clause 3.

It was illogical to suggest that presentation of the data in this way encouraged the prescriber to ignore the safety aspects of administering terazosin. The statement below the chart ('When adding terazosin to a diuretic or other anti-hypertensive agent, dosage reduction and retitration may be needed. Please refer to Summary of Product Characteristics before initiating therapy') clearly reminded the prescriber of this.

These were not isolated data. Other researchers had confirmed these results (Debruyne (1996); Kirby (1998) and Brawer 1993). There was no attempt to minimise the safety issues surrounding administration of terazosin to patients receiving concomitant anti-hypertensive medication. Abbott therefore denied breaches of Clauses 7.2 and 7.7.

Abbott accepted that the numbers of 'controlled hypertensives' receiving concomitant terazosin therapy in the Lowe study was small (n=18; placebo, n=12). Additional supportive data, confirming the minimal effect of terazosin on the blood pressure of controlled hypertensives, were presented by Kirby (1998), n=39; Debruyne (1996), n=14; Brawer (1993),

n=9. The data reported by Lowe were therefore a fair and accurate representation of available data, and were not misleading.

Abbott denied breaches of Clauses 7.2 and 7.6.

PANEL RULING

The Panel noted that Lowe (1994) was a combined analysis of 6 placebo controlled trials to assess the safety of terazosin in normotensive and hypertensive patients with symptomatic BPH. It was noted that whilst inclusion criteria varied in terms of baseline peak flow rates, all of the studies were similar in design; the initial dose was 1mg subsequently titrated upwards to 2, 5, 10 or, in one study, 20mg once daily. Two studies used a fixed-dose titration scheme whereas the others used dose titration to achieve a therapeutic response. The study authors noted that, *inter alia*, judicious stepwise titration of dose levels tended to minimise the incidence of adverse effects. The titration regimen in the six studies reviewed was described as conservative. The study author noted that a more rapid titration could be achieved with the manufacturer's starter pack. The incidence of postural symptoms and dizziness in the terazosin treated group was significant as against placebo.

The Panel considered that its rulings at point A2 were relevant here with regard to the differences between the titration regimen used in Lowe (1994), the dosage recommendation in the SPC and the titration provided for by the starter pack and the effect of these differences upon the data presented. The Panel ruled no breach of Clause 3.2 but considered that the data was nonetheless misleading in this regard and ruled a breach of Clause 7.2 of the Code.

The Panel considered that its rulings at D1 and D2 applied here with regard to the allegation that the chart gave a false impression of the side-effect profile and further that there were no problems with hypotension. The chart had to be considered in the overall context of the page. Breaches of Clauses 7.2 and 7.7 were ruled.

The Panel noted that the number of patients in the controlled hypertensive group was small. Whilst the data might be accurate and representative of a larger body of data the Panel considered that patient numbers ought to have been included as the small patient population was of relevance to the failure to achieve statistical significance. The Panel considered that the bar chart, in this regard, was misleading and unbalanced as alleged and ruled breaches of Clauses 7.2 and 7.6 of the Code.

E Detail aid – alleged breach of Clause 2

COMPLAINT

Yamanouchi stated that, overall, it considered that Abbott's:

- flagrant and repeated use of non-comparable data, in a manner which was clearly designed to give the wrong impression to a busy doctor of the efficacy of Hytrin BPH compared with tamsulosin and other products;
- repeated use of efficacy data which were derived from studies which had used a titration schedule which was inconsistent with the particulars listed in the SPC;
- encouragement provided in this detail aid for doctors to prescribe terazosin to patients who were on anti-hypertensive treatment, without any reference to the SPC warnings;
- statement that the product had no clinically significant effect on blood pressure, despite a number of warnings in the SPC to postural hypotension and related effects;

were activities which discredited the industry.

With a field force of 60-70 representatives making approximately three GP calls per day, this grossly misleading detail aid was being shown to around 1000 GPs each week. The medical profession was very busy. Doctors had little time to see representatives and consequently, as stated earlier, had to rely on the integrity and ethics of the industry and on adherence by the industry to the Code. They had neither the time, nor always the specialist knowledge, to question the bold headings and visual presentations of so-called facts, comparisons and statements in detail aids.

It was Yamanouchi's contention, therefore, that:

- if clinicians understood the wide-ranging issues behind the repeated visual presentations of such incongruous data;
- were aware of the continued use of data from studies where the titration dosages were inconsistent with the SPC;
- were aware of the important warning in the SPC concerning prescribing terazosin to treated hypertensive patients;
- realised the number of warnings about postural hypotension in the SPC despite an assurance by Abbott that the product had no clinically significant effect on BP in normotensive patients;

they would consider this detail aid brought discredit upon, and reduced confidence in, the pharmaceutical industry.

Yamanouchi, therefore, alleged that the detail aid was in breach of Clause 2.

RESPONSE

In summary, Abbott stated that:

1 The detail aid was used to promote Hytrin BPH to consultant urologists, and their senior colleagues who were experienced clinicians, well versed in available therapeutic options, existing therapeutic issues and data analysis.

2 There had been no clinician initiated issues raised about this item to date, nor had the sales force reported any objections to the presentation or content of these data.

3 Abbott accepted that, where available, promotional material should present published comparative data in preference to non-comparative data. In the absence

of such data, Abbott believed that the presentation of data from non-comparative studies could be acceptable, providing that this was done in a fair, accurate, and balanced manner, with no attempt to mislead. Abbott believed that the data in this promotional item were presented in this manner.

4 Excluding one reference to 'Data on file', the data presented in this item had been fully peer reviewed, accepted for publication, and were independently written by eminent opinion leaders in this therapeutic area.

5 The dosages of terazosin used in the studies referenced within this piece were all licensed doses for the treatment of BPH and were consistent with the marketing authorization for Hytrin BPH.

6 Abbott did not accept that any data in this item presented a serious safety issue. Representative data were presented on the effect of terazosin on the blood pressure of normotensive and controlled hypertensive patients, and a clear statement drawing the attention of the prescriber to the cautions contained within the SPC was included.

Abbott refuted all of the allegations made by Yamanouchi of numerous breaches of the Code and further denied a breach of Clause 2.

PANEL RULING

Clause 2 required that materials associated with promotion must never be such as to bring discredit upon or reduce confidence in the pharmaceutical industry. The supplementary information stated that a ruling of a breach of Clause 2 was a sign of particular censure and was reserved for such circumstances. The Panel considered that it was very important that companies were clear and accurate about studies presented in promotional material. The Panel was concerned about the rulings of breaches in relation to safety data. However, on balance, the Panel did not consider that the material was such to merit a ruling of a breach of Clause 2 and no breach of that clause was ruled.

Complaint received **17 September 1999**

Case completed **6 December 1999**

CASE AUTH/928/9/99

RECKITT & COLMAN v ROCHE CONSUMER HEALTH

Rennie Duo journal advertisement

Reckitt & Colman complained about a journal advertisement for Rennie Duo (calcium carbonate, magnesium carbonate, sodium alginate) placed by Roche Consumer Health which featured a photograph of a pregnant woman. The text discussed the treatment of reflux in pregnancy, stating, *inter alia*, that 'Rennie Duo contains calcium and magnesium based antacids with little sodium, making it a suitable treatment for heartburn and acid indigestion throughout pregnancy'.

It was alleged that promoting Rennie Duo for use in pregnancy was misleading, as the summary of product characteristics (SPC) did not state that it was so indicated. In addition the SPC stated that 'As far as is known, if taken as instructed the use of Rennie Duo during pregnancy and lactation is not hazardous to either the foetus or infant' which did not warrant a positive promotion for use in pregnancy. In the Panel's view Rennie Duo was indicated for the symptomatic treatment of reflux and hyperacidity whatever the cause. There was no prohibition or restriction on the use of the product in pregnancy. The Panel noted that in the prescribing information the words 'As far as is known' had been omitted from the pregnancy statement as it appeared in the SPC. The Panel did not consider that this materially altered the statement. The Panel did not consider that promoting the use of Rennie Duo for the treatment of reflux in pregnancy was outside the terms of the product's marketing authorization or inconsistent with its SPC. No breach of the Code was ruled.

It was also alleged that the advertisement would mislead general practitioners into believing the product was low in sodium according to normal accepted standards such as those set in the British National Formulary (BNF). The sodium content of Rennie Duo was 120mg (5.2mmol) per 10ml. The Panel noted that with regard to aluminium and magnesium containing antacids, the BNF added the term 'low Na^+' (low sodium) to the description of those products which had a sodium content of less than 1mmol per tablet or 10ml dose. The advertisement referred to the product containing 'little sodium'. The Panel considered that the phrase 'little sodium' was sufficiently similar to 'low sodium' such that a reader might reasonably infer that Rennie Duo was a 'low sodium' product as defined in the BNF. This was not so. The Panel ruled that the phrase was misleading and in breach of the Code.

Reckitt & Colman Products Limited complained about an advertisement for Rennie Duo (calcium carbonate, magnesium carbonate, sodium alginate) by Roche Consumer Health which appeared as a double page spread in Pulse, 11 September 1999.

The left hand page of the advertisement featured the photograph of a pregnant woman looking at a reflection of herself in a full length mirror beneath the heading 'Double Trouble'. On the right hand page, beneath the heading '*Duo*ble Solution', was text which discussed the treatment of reflux in pregnancy with Rennie Duo stating that 'Rennie Duo contains calcium and magnesium based antacids with little sodium, making it a suitable treatment for heartburn and acid indigestion throughout pregnancy.'

Reckitt & Colman marketed Gaviscon.

1 Alleged promotion of an unlicensed indication

COMPLAINT

Reckitt & Colman noted that the advertisement as a whole in its imagery and its wording was clearly and specifically promoting the product for use in heartburn in pregnancy.

The summary of product characteristics (SPC) for the product did not contain the claim that it was indicated for use in heartburn in pregnancy and stated in section 4.6 'As far as is known, if taken as instructed the use of Rennie Duo during pregnancy and lactation is not hazardous to either the foetus or infant'.

This particular of the SPC did not warrant a positive promotion for use in pregnancy. A normal reading of this statement would imply no more than that no adverse reports had been received of risk to foetus or infant when the product was taken in pregnancy. The SPC did not go further and positively state that Rennie Duo was indicated for use in heartburn in pregnancy. Accordingly the positive promotion of the product for heartburn in pregnancy was not in accordance with the SPC or in accordance with the indications allowed for the product.

Additionally, the text in the Rennie Duo Product Information included in the advertisement contained the statement: 'Rennie Duo, if taken as recommended is not hazardous to either foetus or infant during pregnancy or lactation'. This was not in accordance with the statement in the SPC.

In addition Reckitt & Colman considered that the advertisement would mislead general practitioners into believing the product had been specifically authorized for use in heartburn in pregnancy and that the SPC indicated the use of the product for heartburn in pregnancy.

Breaches of Clauses 3.2 and 7.2 were alleged.

RESPONSE

Roche Consumer Health noted that Reckitt & Colman had not previously raised any objections on the basis that claims for use of Rennie Duo in pregnancy were not in accordance with the SPC. It was somewhat surprised that this was not brought to its attention before the complaint was taken to the Authority.

Roche Consumer Health pointed out that the advertisement was one of a series which illustrated different occasions when heartburn might occur. As the advertisement at issue was the first of the series to

be published, it might give the impression that Roche Consumer Health was focusing its promotional activities on use during pregnancy. This was not the case.

Pregnancy was mentioned in a number of places in the Pulse advertisement as follows:

'One of the lesser joys of pregnancy is reflux. A problem which grows with the baby. Roche Rennie Duo treats reflux, effectively and fast'.

'Rennie Duo contains calcium and magnesium based antacids with little sodium, making it a suitable treatment for heartburn and acid indigestion throughout pregnancy.

So next time you see a patient who is eating for two, consider the benefits of a prescription for dual-action Rennie Duo'.

Roche Consumer Health stated that the indications for Rennie Duo were for use in adults over 12 years of age for the symptomatic treatment of complaints resulting from gastro-oesophageal reflux and hyperacidity, such as regurgitation and heartburn. It considered that the indication section of the SPC would include reflux, whatever the cause, and would include heartburn occurring during pregnancy.

In addition, the advice for use in pregnancy and lactation, section 4.6 of the SPC, was 'As far as is known, if taken as instructed the use of Rennie Duo during pregnancy and lactation is not hazardous to either the foetus or infant'. It believed that anyone referring to this section of the SPC would take it to mean that the product was safe for use during pregnancy. Therefore, the SPC supported use of the product for reflux in pregnancy both within the general indication of reflux and from the point of view of safety. It did not believe that the advertisement was inconsistent with the SPC on this basis.

Roche Consumer Health submitted that there was no medical reason for thinking that Rennie Duo might be unsuitable in pregnancy, since both Rennie tablets (calcium and magnesium carbonates) and Gaviscon (sodium alginate, calcium carbonate and sodium bicarbonate) were indicated for use in pregnancy. Sodium alginate was also approved as an additive in foods. The Medicines Control Agency (MCA) also did not seem to have any medical concerns about use during pregnancy when approving the labelling for the product. The medical assessor had allowed the statement 'These doses may also be used during pregnancy and breast feeding' under the dosing instructions on the label.

Roche Consumer Health stated that it had tried to provide an accurate précis of the product information. The omission of the words 'As far as is known' would not seem to have a significant effect on the value of the information provided. Most statements of this kind could reasonably be prefaced with 'As far as is known', implying that one never had as much data as one would like in an ideal world.

PANEL RULING

The Panel noted that in the prescribing information Rennie Duo was stated to be a general sales list medicine restricted to pharmacy only. The Panel firstly had to decide whether the advertisement was subject to the Code. Clause 1.1 of the Code provided that it applied *inter alia* to the promotion of medicines to members of the UK health professions. The Panel noted that the advertisement had appeared in Pulse, a journal directed at general practitioners. The text discussed the pharmacological action of the medicine and referred to the benefits of a prescription. In the opinion of the Panel the advertisement sought to encourage health professionals to prescribe Rennie Duo and was thus subject to the Code.

The Panel noted that the Rennie Duo SPC stated that it was indicated for the symptomatic treatment of complaints resulting from gastro-oesophageal reflux and hyperacidity, such as regurgitation and heartburn. In the Panel's view this was a wide, unqualified indication and so would include all reflux and hyperacidity whatever the cause. Section 4.6 headed 'Use during pregnancy and lactation' stated that 'As far as is known, if taken as instructed the use of Rennie Duo during pregnancy and lactation is not hazardous to either the foetus or infant.' There was thus no prohibition or restriction on the use of Rennie Duo in pregnancy.

The Panel noted that Clause 4.2 of the Code stated that, *inter alia*, prescribing information must contain a succinct statement of precautions relevant to the indications in the advertisement, giving, in an abbreviated form, the substance of the relevant information in the SPC. The Panel noted that in the prescribing information, the words 'As far as is known' had been omitted from the pregnancy statement as it appeared in the SPC. The Panel did not consider that this materially altered the statement.

The Panel did not consider that promoting the use of Rennie Duo for the treatment of reflux in pregnancy was outside the terms of the product's marketing authorization or inconsistent with its SPC. No breaches of Clauses 3.2 and 7.2 were ruled.

2 Claim 'Contains ... little sodium'

COMPLAINT

Reckitt & Colman alleged that the advertisement would mislead general practitioners into believing the product was low in sodium according to normal accepted standards of measurement. The advertisement stated 'Rennie Duo contains calcium and magnesium based antacids with little sodium, making it a suitable treatment for heartburn and acid indigestion throughout pregnancy.'

The British National Formulary (BNF), which set out formulation standards and guidelines for the medical profession, specified that in order for a product to be able to claim that it was low in sodium it must contain no more than 23mg/10ml. The amount of sodium present in Rennie Duo was 120mg/10ml. Clearly, by the standards used by the medical profession Roche Consumer Health was unable to claim that the product was low in sodium.

Reckitt & Colman submitted that the statement was misleading as it implied that Rennie Duo was 'low in

sodium' according to the accepted standard of measurement, which was incorrect. A breach of Clause 7.2 was alleged.

RESPONSE

Roche Consumer Health noted that the advertisement mentioned sodium once. It stated 'Rennie Duo contains calcium and magnesium based antacids with little sodium…'. The company stated that it had never made any statement that Rennie Duo was a low-sodium product as defined by the BNF and it did not consider that the advertisement would mislead doctors into believing that the product was in this category. In the above statement it wanted partly to convey the message that the antacid properties of Rennie Duo were not based on sodium-containing antacids. Roche Consumer Health had already discussed this point with the MCA which advised that it would prefer the term 'little available sodium' and the company had agreed that it would use this term in future promotional material.

Roche Consumer Health pointed out that the sodium content of Rennie Duo was similar to other products in this class (for example, Rennie Duo contained 120mg sodium per 10ml dose, Liquid Gaviscon contained 142mg per 10ml dose and Gaviscon Advance contained 53mg per 5ml dose). It was worth noting that Reckitt & Colman also made similar claims for the sodium content of Liquid Gaviscon. An advertisement for Gaviscon Advance that appeared in Chemist and Druggist 25 July 1998, stated that Gaviscon Advance 'is even lower in sodium than regular Liquid Gaviscon'. This was clearly implying that Liquid Gaviscon was low in sodium and that Gaviscon Advance was even lower.

PANEL RULING

The Panel noted from the SPC that the sodium content of Rennie Duo was 120mg (5.2mmol) per 10ml. Sodium came not only from one of the active ingredients, sodium alginate, but also from the excipients sodium bicarbonate, sodium saccharin and sodium propylparahydroxybenzoate. Section 4.4 of the SPC, 'Special warnings and precautions for use' drew attention to the sodium content and stated that it should be taken into consideration when treating patients on a restricted sodium diet. The section of the SPC which detailed the pharmacokinetic properties of sodium alginate stated that 'After being taken orally, sodium alginate is not converted in the gastrointestinal tract; 80-100% of the ingested quantity is eliminated. The absorption of alginate salts is negligible'.

The Panel noted that the BNF 38, September 1999, with regard to aluminium and magnesium containing antacids, added the term 'low Na^+' (low sodium) to the description of those products which had a sodium content of less than 1mmol per tablet or 10ml dose.

The Rennie Duo advertisement in question referred to the product containing 'little sodium'. The Panel considered that the phrase 'little sodium' was sufficiently similar to 'low sodium' such that a reader might reasonably infer that Rennie Duo was a 'low sodium' product as defined in the BNF. This was not so. The Panel considered that the phrase was misleading as alleged and ruled a breach of Clause 7.2 of the Code.

Complaint received **28 September 1999**

Case completed **22 November 1999**

GENERAL PRACTITIONER v SOLVAY

Mailing offering a gift

A general practitioner complained about a number of mailings from pharmaceutical companies which offered items (Cases AUTH/929/9/99 to AUTH/935/9/99). He subsequently withdrew his complaints as all of the representatives concerned had provided explanations which he had been happy to accept. However, as all the companies had responded by that time the Authority's Constitution and Procedure precluded withdrawal and the complaints had to proceed.

In this case, the complainant had received a mailing for Femoston from Solvay which included a reply paid card (RPC) offering a free torch/toolkit. It was stated that supplies were strictly limited. Readers could tick the appropriate boxes to request the torch/toolkit, more information on Femoston and/or a visit by a representative. Beneath was a space for 'Best time to visit'. The complainant had put 'By appointment only'. He had ticked all the three boxes and dated the RPC 12 July. His complaint was dated 21 September at which time he had not yet received the torch/toolkit. It was alleged that this was proof of his point that there was a tendency to make such offers conditional upon an interview, the complainant having previously complained about this (Case AUTH/815/12/98).

The Panel noted that there was no complaint about the torch/toolkit, merely its delivery. It had cost the company less than £5. The Panel queried its relevance to the practice of medicine, however, and requested that Solvay be advised of its views.

The Panel noted that the complainant had requested a torch/toolkit, more information about Femoston and for the representative to call by appointment. The representative had telephoned the complainant, as requested, to book an appointment. The Panel had no knowledge of what had been said during the telephone call but noted that the complainant should not have been given the impression that delivery of the torch/toolkit was dependent upon seeing the representative. Representatives must not employ any inducement or subterfuge to gain an interview. The Panel noted that the requested item had now been delivered. The Panel considered that the Solvay representative had behaved appropriately. It was not unacceptable for there to be a reasonable delay between doctors requesting items and those items being delivered. The Panel ruled no breach of the Code.

A general practitioner complained about a number of mailings from pharmaceutical companies which offered items (Cases AUTH/929/9/99 to AUTH/935/9/99). The complainant subsequently wrote to withdraw his complaints as the representatives involved had provided explanations which he had been happy to accept. Paragraph 14.1 of the Constitution and Procedure stated that a complaint could be withdrawn by a complainant up until such time as the respondent company's comments on the complaint had been received by the Authority but not thereafter. The responses had been received from all the companies and the complaints therefore had to be considered.

The material in question in this case was a Femoston mailing (ref SOL/106/07/99) which the complainant had received from Solvay Healthcare Ltd. The mailing had included a reply paid card (RPC) offering a free torch/toolkit. It was stated that supplies were strictly limited. Readers could tick the appropriate boxes to request the torch/toolkit, more information on Femoston and/or a visit by a representative. Underneath the tick boxes was a space for the doctor to fill in 'Best time to visit'. The complainant had ticked all three boxes and in the space for 'Best time to visit' had written 'By appointment only'. He had dated the RPC 12 July and his complaint to the Authority was dated 21 September.

COMPLAINT

The complainant stated that so far the torch/toolkit had not been brought to the surgery. In his view this was sufficient proof of the point he had made when he had complained about medical representatives last year (Case AUTH/815/12/98).

The complainant stated that, without doubt, the tendency was to make offers conditional on an interview which he understood was against advice given by the Authority (Offers on reply paid cards, November 1998 Code of Practice Review).

RESPONSE

Solvay stated that the gift offered in the Femoston mailing was a 'Flashlight with toolkit'. This could have been very helpful to general practitioners in a number of relevant situations, for example in the surgery, on night calls or in the car in case of breakdown. The flashlight was supplied complete with batteries and the total unit cost to the company was £3.93. Therefore, the gift met the requirements of Clause 18.2 in that it was both relevant to a general practitioner's work and inexpensive.

Solvay submitted that the RPC met the requirements of Clause 9.7; it bore the Femoston brand name but no further information relating to the use of the medicine. Furthermore, the materials were designed with the requirements of Clause 9.1 firmly in mind.

Solvay stated that the mailing was sent to 7,500 general practitioners with a particular interest in women's health/HRT. The company's general experience was that a mailing would result in 10-20% positive responses. Three thousand flashlights were ordered and it was, therefore, expected that all respondents would receive one of the gifts. The statement that 'Supplies are strictly limited' was included on the RPC in case there was an unexpectedly large demand, because additional units would have been very difficult to obtain. The actual response was such that all doctors who expressed a

wish to receive one of the flashlights would receive one.

Solvay stated that the flashlight was bulky and would have been cumbersome to post (and receive) and it was considered that there was the possibility of damage in transit. Therefore, it was the company's expectation that the majority would be delivered by its representatives. Solvay emphasised that all of its field force was well aware of the requirements of the Code that gifts must be provided to those doctors who wanted them whether or not an interview was granted. The Solvay Healthcare Representative Standard Procedure required that all of its representatives had received a copy of the Code and were familiar with it as it applied to their work.

Solvay noted that the mailing was sent out on 9 July. The complainant obviously dated the card when he received it on 12 July. He returned the card indicating that he wished to receive the gift and moreover that he wished to receive more information on Femoston and wanted a representative to visit him.

The reply paid cards received by Solvay were collated according to representatives' territories and then sent for action to the representative. Sufficient supplies of the flashlights for all respondents were then delivered to the representatives (sent to them on 30 July). A copy of an e-mail informing the representatives that they would receive the items was supplied. Further briefing was not considered necessary because the representatives were well aware of the required procedures.

The region in which the complainant practised was normally covered by a full-time and a part-time representative, but at the time there was a vacancy for a part-timer. The region was not an easy area to cover at the height of the summer and the representative was on holiday for three weeks over this period. Nevertheless, the representative telephoned the complainant on 20 September regarding the information on Femoston and the gift and made an appointment for 27 September when she saw him and delivered the materials. At no time did the complainant state that he had any problem with the mailing or Solvay's response. Furthermore the representative spontaneously confirmed that she would have left the gift for the complainant if he had indicated that this was what he wanted. The representative maintained the high standard of conduct the company required and there was no question of using inducement or subterfuge to gain the interview. Therefore, there was no breach of either Clause 15.2 or 15.3.

In view of all of the above, Solvay was very surprised that the complainant then wrote to the Authority on 21 September.

In conclusion, Solvay did not consider that there was a case to answer. Offers of a gift, which met Code requirements, further information on its product and the opportunity to meet a representative were made and accepted by the complainant. In relation to Solvay's activities in this matter, it was difficult to see exactly what the problem was and the company could only consider that it had been caught up in the general practitioner's overall issue with pharmaceutical companies' promotional activities in relation to the provision of gifts.

PANEL RULING

The Panel noted that there was no complaint about the torch/toolkit, merely its delivery. The Panel noted it cost the company less than £5. The Panel queried its relevance to the practice of medicine, however, and requested that Solvay be advised of its views.

The Panel noted that the complainant had requested a torch/toolkit, more information about Femoston and for the representative to call by appointment. The representative had telephoned the complainant, as requested, to book an appointment. The Panel had no knowledge of what had been said during the telephone call but noted that the complainant should not have been given the impression that delivery of the torch/toolkit was dependent upon seeing the representative. In all circumstances involving the delivery of an item representatives had to bear in mind the requirements of Clause 15.3 that they must not employ any inducement or subterfuge to gain an interview. The Panel noted that the requested item had now been delivered.

The Panel considered that the Solvay representative had behaved appropriately. It was not unacceptable for there to be a reasonable delay between doctors requesting items and those items being delivered. The Panel ruled no breach of Clause 15.3 of the Code.

Complaint received **27 September 1999**

Case completed **22 November 1999**

GENERAL PRACTITIONER v SCHERING-PLOUGH

Mailing offering a gift

A general practitioner complained about a number of mailings from pharmaceutical companies which offered items (Cases AUTH/929/9/99 to AUTH/935/9/99). He subsequently withdrew his complaints as all of the representatives concerned had provided explanations which he had been happy to accept. However, as all the companies had responded by that time the Authority's Constitution and Procedure precluded withdrawal and the complaints had to proceed.

The material in question in this case was an Elocon reply paid card (RPC) which the complainant had received from Schering-Plough. The RPC offered a free first-aid kit. Underneath a tick box to request the item was a space for the doctor to fill in the most convenient date and time for a visit from a representative. The complainant had ticked the box and written 'Please leave at reception'. He had dated the RPC 2 July and his complaint to the Authority was dated 21 September at which time he had not yet received the first-aid kit. It was alleged that this was proof of his point that there was a tendency to make such offers conditional upon an interview, the complainant having previously complained about this (Case AUTH/815/12/98).

The Panel noted that there was no complaint about the first-aid kit, merely its delivery. It was relevant to the practice of medicine and had cost the company less than £5. The Panel noted that the complainant had asked for a first-aid kit to be left at reception.

The Panel noted that the delay in delivering the first-aid kit was because Schering-Plough was awaiting further supplies. The complainant should by now have had a kit delivered. Representatives must not employ any inducements or subterfuge to gain an interview. The provision of a promotional aid must not be conditional on seeing the recipient. The Panel considered that the Schering-Plough representative had behaved appropriately. It was not unacceptable for there to be a reasonable delay between doctors requesting items and those items being delivered. The Panel ruled no breach of the Code.

A general practitioner complained about a number of mailings from pharmaceutical companies which offered items (Cases AUTH/929/9/99 to AUTH/935/9/99). The complainant subsequently wrote to withdraw his complaints as the representatives involved had provided explanations which he had been happy to accept. Paragraph 14.1 of the Constitution and Procedure stated that a complaint could be withdrawn by a complainant up until such time as the respondent company's comments on the complaint had been received by the Authority but not thereafter. The responses had been received from all companies and the complaints therefore had to be considered.

The material in question in this case was a Elocon reply paid card (RPC) (ref ELO/99-249) which the complainant had received from Schering-Plough Ltd. The RPC was in support of Schering-Plough's dermatological products and offered a free first-aid kit. Readers could tick the appropriate box to request the first-aid kit. Underneath the tick box was a space for the doctor to fill in the most convenient date and time for a visit from the Schering-Plough representative. The complainant had ticked the box and written 'Please leave at reception'. He had dated the RPC 2 July and his complaint to the Authority was dated 21 September.

COMPLAINT

The complainant stated that so far the first-aid kit had not been brought to the surgery. In his view this was sufficient proof of the point he had made when he had complained about medical representatives last year (Case AUTH/815/12/98).

The complainant stated that, without doubt, the tendency was to make offers conditional on an interview which he understood was against advice given by the Authority (Offers on reply paid cards, November 1998 Code of Practice Review).

RESPONSE

Schering-Plough stated that it was certainly not the case that the offer of a first-aid kit was conditional on granting an interview. At no time did the representative use, or attempt to use, the RPC, and offer of a first-aid kit as an inducement to see the general practitioner in question or any other healthcare professional at the surgery.

Specific guidance, both verbal and written, had been given to all the representatives on the appropriate use of RPCs and promotional items such as this one. In addition the representatives were further reminded of the need to comply with the Code when supplying these particular first-aid kits.

A copy of the cycle briefing document covering the period when this activity was initiated was provided. Under the section 'Key issues' subheading 'Reply Paid Cards' there was a highlighted section which stated; 'As you know, in accordance with ABPI regulations it is important to note that a doctor is not obliged to see you when you deliver an item and if requested you should leave the item'.

The reason that the complainant did not receive his first-aid kit was due to an over subscription to the offer. Four thousand first-aid kits were originally ordered. These were allocated to the representatives for delivery to interested doctors. So high was the response that stocks were rapidly exhausted and more had to be ordered. The original requests were filled on a 'first come, first served' basis. Three thousand of the second tranche were already with the representatives who were currently delivering them. Schering-Plough fully intended to honour its offer to

those doctors who requested one of the first-aid kits – without making the offer conditional on an interview.

It was unfortunate that this unexpected demand meant that the complainant had a delay in receiving his kit. The representative should have, by now, delivered the first-aid kit to the surgery, with Schering-Plough's apologies for the delay.

The RPCs were not mailed directly to general practitioners; instead they were allocated to sales representatives, who handed them out to practices and at educational meetings.

This was the case with the complainant's practice. The local representative held a meeting there, handed out her remaining first-aid kit to the first doctor who asked for one and left RPCs with the practice manager to be passed on to any other interested doctors.

The cost of the first-aid kits to the company was £4.95.

Schering-Plough believed that it had acted well within the letter and the spirit of the Code in its handling of this promotional activity. It hoped that the complainant would accept its apologies for the delay in providing the item, and realise that in no way was it making the supply of the kit conditional on an interview.

PANEL RULING

The Panel noted that there was no complaint about the first-aid kit, merely its delivery. It was relevant to the practice of medicine and had cost the company less than £5. The Panel noted that the complainant had asked for a first-aid kit to be left at reception.

The delay in delivering the first-aid kit was because Schering-Plough was awaiting further supplies. The complainant should by now have had a kit delivered. Representatives had to comply with the requirements of Clause 15.3 in that they must not employ any inducements or subterfuge to gain an interview. The provision of a promotional aid must not be conditional on seeing the recipient.

The Panel considered that the Schering-Plough representative had behaved appropriately. It was not unacceptable for there to be a reasonable delay between doctors requesting items and those items being delivered. The Panel ruled no breach of Clause 15.3 of the Code.

The Panel was concerned that the representatives' briefing notes implied that, in the absence of an interview, the need was only to leave gifts for doctors if requested to do so. The Panel accepted that items offered on mailings were often delivered by representatives but noted that if a doctor was not available, or did not want to see a representative, the item had to be left, regardless of whether or not there was a request to do so, otherwise it became an inducement to gain an interview. The Panel requested that its concerns be passed on to Schering-Plough.

Complaint received **27 September 1999**

Case completed **22 November 1999**

GENERAL PRACTITIONER v SANOFI WINTHROP and BRISTOL-MYERS SQUIBB

Mailing offering a gift

A general practitioner complained about a number of mailings from pharmaceutical companies which offered items (Cases AUTH/929/9/99 to AUTH/935/9/99). He subsequently withdrew his complaints as all of the representatives concerned had provided explanations which he had been happy to accept. However, as all the companies had responded by that time the Authority's Constitution and Procedure precluded withdrawal and the complaints had to proceed.

The material in question in this case was an Aprovel mailing which the complainant had received from Sanofi Winthrop and Bristol-Myers Squibb. The mailing had included a reply paid card (RPC) offering a free obese sphygmomanometer cuff. Underneath the tick boxes to request the obese cuff and more information on Aprovel was a space for the doctor to fill in his name and signature which was followed by a section 'The most convenient time for a representative to call is' under which two statements appeared, 'There is no obligation to grant a representative an interview' and 'Please indicate Mon-Fri am/pm'. The complainant had written 'Please leave at desk at reception' on the RPC which was not dated. He had not yet received the cuff. It was alleged that this was proof of his point that there was a tendency to make such offers conditional upon an interview, the complainant having previously complained about this (Case AUTH/815/12/98).

The Panel noted that there was no complaint about the obese cuff, merely its delivery. It was relevant to the practice of medicine and had cost less than £5. The Panel noted that the RPC supplied by the complainant was slightly different to that supplied by the respondent companies.

The Panel noted that the cuff was not delivered to the complainant until early October. This was due to the cycle worked by the representatives. Representatives must not employ any inducements or subterfuge to gain an interview. The provision of a promotional aid must not be conditional on seeing the recipient. The RPC clearly stated that there was no obligation to grant the representative an interview. The Panel considered that the representative had behaved appropriately. It was not unacceptable for there to be a reasonable delay between doctors requesting items and those items being delivered. The Panel ruled no breach of the Code.

A general practitioner complained about a number of mailings from pharmaceutical companies which offered items (Cases AUTH/929/9/99 to AUTH/935/9/99). The complainant subsequently wrote to withdraw his complaints as the representatives involved had provided explanations which he had been happy to accept. Paragraph 14.1 of the Constitution and Procedure stated that a complaint could be withdrawn by a complainant up until such time as the respondent company's comments on the complaint had been received by the Authority but not thereafter. The responses had been received from all the companies and the complaints therefore had to be considered.

The material in question in this case was an Aprovel mailing (ref APR/0799/467) which the complainant had received from Sanofi Winthrop Limited and Bristol-Myers Squibb Pharmaceuticals Limited. The mailing had included a reply paid card (RPC) offering a free obese sphygmomanometer cuff. Readers could tick the appropriate boxes to request the obese cuff, and more information on Aprovel. Underneath the tick boxes was a space for the doctor to fill in his name and signature which was followed by a section 'The most convenient time for a representative to call is' under which two statements appeared, 'There is no obligation to grant a representative an interview' and 'Please indicate Mon-Fri am/pm'. The complainant had written 'Please leave at desk at reception' on the RPC which was not dated.

COMPLAINT

The complainant stated that so far the obese cuff had not been brought to the surgery. In his view this was sufficient proof of the point he had made when he had complained about medical representatives last year (Case AUTH/815/12/98).

The complainant stated that, without doubt, the tendency was to make offers conditional on an interview which he understood was against advice given by the Authority (Offers on reply paid cards, November 1998 Code of Practice Review).

RESPONSE

A joint response was submitted on behalf of Bristol-Myers Squibb and Sanofi Winthrop.

The companies stated that the mailing offering a sphygmomanometer cuff for the measurement of blood pressure in obese patients was sent to 14,000 general practitioners on 16 July 1999. The item was clearly relevant to the practice of medicine and cost less than £5.

The mailing was sent from a professional mailing company, and the RPC was addressed to the Assistant Product Manager at Sanofi Winthrop. As part of the mailing service the RPCs returned automatically to the mailing company (ie not to the Sanofi Winthrop address on the RPC) which then forwarded them to the representative responsible for that territory. Upon receipt of the RPC from the mailing house the representative was then expected to make arrangements to deliver items to the requesting physician.

The companies submitted that the representatives were instructed to deliver the items to all requesting

physicians and, as was made clear in the RPC, were instructed not to make delivery of the item conditional upon an interview with the general practitioner. 8,000 cuffs were purchased in the expectation that this would exceed demand based on experience of the likely response rate to such mailings.

A copy of the memorandum from the companies to the representatives dated 17 August 1999 was enclosed. Ten cuffs were made available to each representative in the first instance and this was expected to fulfil the requests received for their territory. If necessary representatives could request additional supplies.

Although the representatives and the mailing house did not keep records of when and to whom cuffs had been delivered, a number of cuffs had been distributed to date and everyone who requested one would receive one.

The companies' records indicated that the RPC from the complainant was received at the mailing house on 16 August 1999. The request was relayed to the responsible representative at that time. The cuffs were distributed to the representatives shortly after 17 August 1999 and the cuff was in fact delivered to the complainant in early October. The representatives worked on an eight week cycle to cover their geographic territories and therefore a delay of up to eight weeks was normal prior to any delivery.

PANEL RULING

The Panel noted that there was no complaint about the obese cuff, merely its delivery. It was relevant to the practice of medicine and had cost less than £5. The Panel noted that the RPC supplied by the complainant was slightly different to that supplied by the respondent companies.

The Panel noted that the cuff was not delivered to the complainant until early October. This was due to the cycle worked by the representatives. Representatives delivering items had to comply with the requirements of Clause 15.3 that they must not employ any inducements or subterfuge to gain an interview. The provision of a promotional aid must not be conditional on seeing the recipient. The RPC clearly stated that there was no obligation to grant the representative an interview.

The Panel considered that the representative had behaved appropriately. It was not unacceptable for there to be a reasonable delay between doctors requesting items and those items being delivered. The Panel ruled no breach of Clause 15.3 of the Code.

Complaint received **27 September 1999**

Case completed **22 November 1999**

GENERAL PRACTITIONER v ASTRAZENECA

Mailing offering a gift

A general practitioner complained about a number of mailings from pharmaceutical companies which offered items (Cases AUTH/929/9/99 to AUTH/935/9/99). He subsequently withdrew his complaints as all of the representatives concerned had provided explanations which he had been happy to accept. However, as all the companies had responded by that time the Authority's Constitution and Procedure precluded withdrawal and the complaints had to proceed.

The material in question in this case was a letter which the complainant had received from Royce Medical in association with AstraZeneca. The letter offered year 2000 diaries and included a tear off slip. Recipients could tick the slip to request five different types of diaries. Also included was a space for the doctor to fill in 'Best time to deliver'. The complainant had requested an A5 week to view diary and in the space for 'Best time to deliver' had written 'Please leave in reception'. He had not yet received the diary. It was alleged that this was proof of his point that there was a tendency to make such offers conditional upon an interview, the complainant having previously complained about this (Case AUTH/815/12/98).

The Panel noted that there was no complaint about the diary, merely its delivery. It was relevant to the practice of medicine and had cost the company less than £5.

The Panel noted that there was no evidence that the representative had intended to use the diary as an inducement to gain an interview. Representatives must not make, or appear to make, delivery of a gift conditional on the recipient seeing them. The Panel noted that the diary had now been delivered. The Panel noted the timings in the response from AstraZeneca and considered that the representative had behaved appropriately in relation to the delivery of the diary. It was not unacceptable for there to be a reasonable delay between doctors requesting items and those items being delivered. The Panel ruled no breach of the Code.

A general practitioner complained about a number of mailings from pharmaceutical companies which offered items (Cases AUTH/929/9/99 to AUTH/935/9/99). The complainant subsequently wrote to withdraw his complaints as the representatives involved had provided explanations which he had been happy to accept. Paragraph 14.1 of the Constitution and Procedure stated that a complaint could be withdrawn by a complainant up until such time as the respondent company's comments on the complaint had been received by the Authority but not thereafter. The responses had been received from all the companies and the complaints therefore had to be considered.

The material in question in this case was a letter which the complainant had received from Royce Medical in association with AstraZeneca. The letter offered year 2000 diaries and included a tear off slip. Recipients could tick the slip to request five different types of diaries. Also included was a space for the doctor to fill in 'Best time to deliver'. The complainant had requested an A5 week to view diary and in the space for 'Best time to deliver' had written 'Please leave in reception'.

COMPLAINT

The complainant stated that so far the diary had not been brought to the surgery. In his view this was sufficient proof of the point he had made when he had complained about medical representatives last year (Case AUTH/815/12/98).

The complainant stated that, without doubt, the tendency was to make offers conditional on an interview which he understood was against advice given by the Authority (Offers on reply paid cards, November 1998 Code of Practice Review).

The matter was taken up with AstraZeneca. Royce Medical provided contract representatives to AstraZeneca.

RESPONSE

AstraZeneca submitted that the initiative was instigated by Royce Medical and instructions were issued directly by e-mail to its representatives. The diaries were issued to the representative in question to offer to her doctors as an added value service item only. It was never the intention of Royce Medical that the diaries should be used as an inducement to gain an interview. The letter to the complainant was sent in mid August.

Each representative received an allocation of 40 diaries, which were distributed after receipt by Royce Medical of the consignment on 14 September 1999.

Following receipt of the diaries by the representative she was required to attend a sales conference for the period 20-24 September 1999. The representative had a long-standing lunchtime meeting appointment with the complainant's practice on Friday 1 October 1999. The complainant was not in attendance as he was on study leave. The meeting ran late, the representative had other commitments later that day and in the rush forgot to leave the diary. The representative did not request to see the complainant to deliver the diary on another date.

The representative was informed later that day by her manager that the general practitioner had complained that the diary had not been left for him. The representative contacted the practice manager and agreed she would deliver the diary on Monday 4 October 1999, which she did. A thank you letter from the complainant confirming delivery of the diary was provided. This also acknowledged that the diaries had only been delivered to the representative within the last four weeks.

Thus, there was a gap of approximately 2 1/2 weeks between receipt of the diaries by Royce Medical and delivery by the representative. AstraZeneca did not consider this an unreasonable time lapse.

It was the expressed intention of Royce Medical that all doctors who indicated their desire to receive a diary would receive one as soon as practically possible, it was too early to categorically state that all those who did so would have received their diary. Each diary cost £1.62 including VAT. Only limited quantities of Royce Medical diaries were made available to each representative. It was intended that each doctor could only select and request one diary on the order form. Only one diary per doctor had been issued.

It was company policy for both Royce Medical and AstraZeneca that sales management would normally approve such mailings from representatives to healthcare professionals. Regrettably, on this occasion the representative acted on her own initiative in issuing the letter and an internal investigation was being conducted. In addition, as the responsibility for this diary initiative was solely that of Royce Medical, the inclusion of AstraZeneca's name on the letterhead, unfortunately mis-spelt, was not appropriate or agreed.

AstraZeneca did not accept that the letter sent by the representative could be considered as an inducement or subterfuge to gain an interview with the complainant. Furthermore, there was no evidence that the representative used the diary as an inducement to gain an interview. The company did not therefore accept that there had been any breach of the Code.

PANEL RULING

The Panel noted that there was no complaint about the diary, merely its delivery. It was relevant to the practice of medicine and had cost the company less than £5.

There was no evidence that the representative had intended to use the diary as an inducement to gain an interview but the Panel considered it unfortunate that it had not been left for the doctor at the lunchtime meeting on Friday, 1 October. In all circumstances involving the delivery of a gift, representatives had to bear in mind the requirements of Clause 15.3 that they must not make, or appear to make, its provision conditional on the recipient seeing them. The Panel noted that the diary had been delivered.

The Panel noted the timings in the response from AstraZeneca and considered that the representative had behaved appropriately in relation to the delivery of the diary. It was not unacceptable for there to be a reasonable delay between doctors requesting items and those items being delivered. The Panel ruled no breach of Clause 15.3 of the Code.

The Panel was very concerned that the letter had been issued without the agreement of AstraZeneca. It was very important that pharmaceutical companies knew exactly what their representatives were doing. This included contract representatives. Representatives should be trained and instructed carefully about what they could and could not do in the course of their employment. The Panel noted that AstraZeneca had initiated an internal investigation and in the Panel's view the matter should be dealt with as a priority. The Panel requested that its concerns be made known to the company.

Complaint received **27 September 1999**

Case completed **22 November 1999**

GENERAL PRACTITIONER v GLAXO WELLCOME and BRITANNIA

Mailing offering a gift

A general practitioner complained about a number of mailings from pharmaceutical companies which offered items (Cases AUTH/929/9/99 to AUTH/935/9/99). He subsequently withdrew his complaints as all of the representatives concerned had provided explanations which he had been happy to accept. However, as all the companies had responded by that time the Authority's Constitution and Procedure precluded withdrawal and the complaints had to proceed.

The material in question in this case was a 'Dear Doctor' letter which the complainant had received from Glaxo Wellcome. The letter offered two vials of Crystapen Injection by way of a tear off section which included a space for the doctor's signature together with a space to complete the date and a box for the doctor to tick. There was also a space for the doctor to fill in 'Best time to call: Day … Time …'. The complainant had signed the slip and had written on it 'Please leave at desk'. He had dated the slip 21 July and his complaint to the Authority was dated 21 September, at which time he not yet received the Crystapen. It was alleged that this was proof of his point that there was a tendency to make such offers conditional upon an interview, the complainant having previously complained about this (Case AUTH/815/12/98).

The Panel noted that the Glaxo Wellcome representative had not yet delivered the item. This was due to a combination of the representative's holiday and him subsequently not being in the area to deliver the item. Representatives must not employ any inducement or subterfuge to gain an interview. The Panel considered that the Glaxo Wellcome representative had behaved appropriately. It was not unacceptable for there to be a reasonable delay between doctors requesting items and those items being delivered. The Panel therefore ruled no breach of the Code.

Britannia, whose product Crystapen was, had not been responsible for the mailing and the Director ruled that it had no prima facie case to answer.

A general practitioner complained about a number of mailings from pharmaceutical companies which offered items (Cases AUTH/929/9/99 to AUTH/935/9/99). The complainant subsequently wrote to withdraw his complaints as the representatives involved had provided explanations which he had been happy to accept. Paragraph 14.1 of the Constitution and Procedure stated that a complaint could be withdrawn by a complainant up until such time as the respondent company's comments on the complaint had been received by the Authority but not thereafter. The responses had been received from all the companies and the complaints therefore had to be considered.

The material in question in this case was a 'Dear Doctor' letter dated 19 July 1999 (ref SMT10228/May 1998) which the complainant had received from Glaxo Wellcome UK Limited. The letter offered two vials of Crystapen Injection. The mailing had included a tear off section which included a space for the doctor's signature together with a space to complete the date and a box for the doctor to tick. There was also a space for the doctor to fill in 'Best time to call: Day … Time …'. The complainant had signed the slip and had written on it 'Please leave at desk'. He had dated the slip 21 July and his complaint to the Authority was dated 21 September.

COMPLAINT

The complainant stated that so far the samples had not been brought to the surgery. In his view this was sufficient proof of the point he had made when he had complained about medical representatives last year (Case AUTH/815/12/98).

The complainant stated that, without doubt, the tendency was to make offers conditional on an interview which he understood was against advice given by the Authority (Offers on reply paid cards, November 1998 Code of Practice Review).

* * * * *

Crystapen Injection was a former Glaxo Wellcome product that was now owned by Britannia Pharmaceuticals Ltd. Glaxo Wellcome said that it had continued its practice of making it available for emergency use in meningitis. The matter was taken up with both companies.

Britannia stated that it was not responsible for the mailing. The Director therefore decided that there was no *prima facie* case for Britannia to answer under the Code.

RESPONSE

Glaxo Wellcome submitted that rather than offering a gift, the mailing was offering a starter pack of a medicine, which might be life-saving in meningitis, and which would be expected to be found in a clinician's emergency bag.

The complainant was one of 41 positive responses to the mailing, which had been received by the relevant representative. The normal procedure for a contract representative processing such a positive reply to a mailing within Glaxo Wellcome was that the mailing was initially sent to head office by the replying doctor, from where it was redirected to the representative concerned, often via their line manager. This process in itself took a variable but not insignificant amount of time, perhaps up to a week or two. In this

particular instance, the representative was also on holiday during August, thus possibly prolonging the period before which he received the complainant's positive reply. The representative stated that he received the reply in late August.

Since receiving it along with the other 40 positive replies, the representative prioritised the delivery of starter packs according to his geographical work plan. He had visited the complainant's area on 25 August, and since his area of responsibility included all of Cornwall, he had not yet re-visited the area because of his work commitments to the whole locality. As at 30 September he had in fact been able to deliver 9 starter packs, leaving a further 32 to be delivered in the coming weeks, of which the complainant's was one. A copy of the representative's geographical workplan was provided as was a copy of the list of doctors in the region who were sent the mailing.

The representative received a copy of the mailing prior to it being sent out to the doctors in his locality. He was aware of the requirements in the Code regarding starter pack delivery, and had been briefed on how such a mailing should be handled under the Code.

Of the 9 he had so far delivered, all had been handed directly to the clinician, some because of appointments specifically arranged, and others because of arrangements previously made (eg surgery meetings). It had always been the representative's intention to deliver the starter pack to the complainant by the method requested when he next visited the locality. Everyone who had requested a starter pack would receive one.

Glaxo Wellcome understood why the complainant might be concerned that he had not yet received his starter pack but considered that it had acted entirely properly in this matter, and had no intention of providing the pack to secure an interview.

PANEL RULING

The Panel noted that the Glaxo Wellcome representative had not yet delivered the item. This was due to a combination of the representative's holiday and him subsequently not being in the area to deliver the item. Representatives delivering items had to comply with the requirements of Clause 15.3 in that they must not employ any inducement or subterfuge to gain an interview. The provision of a gift, starter pack or a sample must not be conditional on seeing the recipient. Clearly representatives had to make sure that they obtained signed, dated, written requests for samples as required by Clause 17.3 of the Code and that samples delivered by representatives were handed to the health professional requesting them or persons authorized to receive them on their behalf.

The Panel considered that the Glaxo Wellcome representative had behaved appropriately. It was not unacceptable for there to be a reasonable delay between doctors requesting items and those items being delivered. The Panel therefore ruled no breach of Clause 15.3 of the Code.

Complaint received **27 September 1999**

Case completed **22 November 1999**

CASE AUTH/937/10/99

GENERAL PRACTITIONER v MERCK SHARP & DOHME

Zocor journal advertisement

A general practitioner complained about a journal advertisement for Zocor issued by Merck Sharp & Dohme.

The complainant was concerned that the use of a gaudy neon light to carry the claim 'Zocor – Proven Efficacy' was inappropriate. The Panel did not consider that this was unacceptable and ruled no breach.

The claim in neon lights was followed by 'up to 9 out of 10 CHD patients can reach the LDL-C goal of <3mmol/l'. The complainant alleged that this was all encompassing and did not define the dose. In the complainant's opinion the emphasis of the supporting evidence was for 40mg Zocor only and then only in post myocardial infarct patients. The Panel considered that overall the claim was misleading, exaggerated and not capable of substantiation. Breaches of the Code were ruled.

The Panel ruled no breach with regard to an allegation that the reference to the lipid parameters was inconsistent and unclear.

A general practitioner complained about a journal advertisement for Zocor (simvastatin) issued by Merck Sharp & Dohme Limited. The advertisement in question was understood to be that which appeared in GP, 8 October 1999 (ref 08-00 ZCR.99.GB.70159.J.b.). The advertisement was headed 'Zocor – Proven Efficacy' followed by 'up to 9 out of 10'. These claims were represented in neon lights and were followed by the claim 'CHD patients can reach the LDL-C goal of <3mmol/l'.

COMPLAINT

The complainant stated that the advertisement carried a message in the form of a gaudy neon light that created an impression that the practice of medicine was now reduced to a bargain basement activity worthy of headlines one normally associated with cheap roadside cafes and bars!

To make matters worse the advertisement was also confusing with regard to the following points:

1 The message conveyed was all encompassing and did not define the specific dose of Zocor to which it referred. In the complainant's opinion, the emphasis of the supporting evidence was for the 40mg Zocor only and then only in post-MI patients.

2 The reference to lipid parameters was also inconsistent and unclear. The advertisement related to CHD patients and in this context the Zocor data sheet specifically referred to total cholesterol whereas the advertisement emphasised LDL-cholesterol goals.

3 Having reviewed the evidence, the complainant considered that the 90% figure cited was misleading. The achievement of goals was nowhere near 90%, a fact that was also conveniently not referred to by Merck Sharp & Dohme representatives. Surely this was a gross exaggeration?

4 The complainant's most grave concern was that the wording of the advertisement clearly guaranteed more than the product could deliver. Again exaggeration appeared to be the name of the game.

The complainant stated that general practitioners, such as himself, did not find this type of billboard advertising helpful, particularly when the message was misleading, confusing and presented only what suited.

When writing to Merck Sharp & Dohme the Authority drew attention to Clauses 7.2, 7.3, 7.6, 7.8 and 9.1 of the Code of Practice.

RESPONSE

Merck Sharp & Dohme regretted the complainant's perspective regarding the neon sign but considered that it was a highly personalised view. The concept of the neon sign style in the company's prior advertisement had undergone research and was found to be generally acceptable. Merck Sharp & Dohme therefore regarded the complainant's opinion as a personal view and not representative of the medical community as a whole.

Merck Sharp & Dohme submitted that the advertisement made it quite clear that it was up to 9 out of 10 patients who could get to the stated LDL-C goal of <3mmol/l: Merck Sharp & Dohme did not claim that all patients at all doses could achieve these levels. Supporting evidence for the 40mg of Zocor was provided, wherein indeed over 9 out of 10 patients did reach the stated LDL-C goal, as well as evidence showing that over 70% of patients on 10mg of Zocor could get to the specified goals (Pederson *et al* (1999)); Heart Protection Study (1999); Giles *et al* (1998)).

The advertisement specified both total cholesterol and LDL-cholesterol as practitioners differed in their chosen measurement. Both were relevant but general practitioners interested in lipid management with patients with coronary artery disease would be more interested in the LDL-C goal. As would be seen in the data provided, Zocor was able to meet both the total cholesterol and LDL-cholesterol targets itemised in this advertisement.

Merck Sharp & Dohme considered that the 90% figure cited was not misleading. The data clearly showed that the highest dose would achieve this stated goal and the 'up to' related to the fact that lower doses still could reach the stated goals, albeit in lower numbers.

Merck Sharp & Dohme submitted that the advertisement was not exaggerated or misleading.

The data supported the contention that Zocor was able to lower LDL-C and total cholesterol to the new recommendations from the British Cardiac Society, the British Hyperlipidemia Association and the British Hypertension Society. Using the licensed dose range of 10-40mg the great majority of patients did achieve these pre-specified goals and Merck Sharp & Dohme had supported this claim with data from Scandinavia and the UK.

PANEL RULING

The Panel noted the complainant's concerns about the use of the neon light in the advertisement. The Panel considered that the advertisement was not unacceptable in this regard. It was not likely to cause offence and the Panel therefore ruled no breach of Clause 9.1 of the Code.

The rest of the complaint related to the claim 'up to 9 out of 10 CHD patients can reach the LDL-C goal of <3mmol/l'. The claim was attributed to Pedersen, European Atherosclerosis Society, Athens May 1999. The claim was followed by an obelus which referred to new joint recommendations from the British Cardiac Society, the British Hyperlipidaemia Association and the British Hypertension Society (endorsed by the British Diabetic Association) of total cholesterol <5mmol/l and LDL-C <3mmol/l.

Merck Sharp & Dohme provided data to support the claim. Pedersen *et al* (1999) was an abstract reporting a study carried out in patients with acute myocardial infarction (n=112) or unstable angina (n=39) and LDL-C ≥3mmol/l who were allocated to one of two strategies of lipid intervention. Both groups had dietary counselling, one group received simvastatin 40mg daily from the day of randomisation whilst the other started simvastatin after 3 months if LDL-C was still ≥ 3mmol/l. At six months 82% of patients in the deferred treatment group had reached target. 90% of patients in the immediate treatment group had reached target after 3 months and remained on target at six months.

A study by Giles *et al* (1998) showed that 83% of post myocardial infarct patients achieved a total cholesterol of less than 5.2mmol/l. The mean total cholesterol at entry was 5.97mmol/l. The choice of lipid lowering medication depended on the triglyceride level but in practice the overwhelming majority of patients were treated with simvastatin at a dose of 10mg daily. Merck Sharp & Dohme had undertaken a subgroup analysis of 229 patients who had been so treated. This analysis was presented as data on file and showed that 10mg of simvastatin achieved the stated LDL-C target of 3mmol/l in 75% of patients and total cholesterol target of 5mmol/l in 72% of patients. It was not stated what sub-group had been analysed or how it had been identified. Nor was it stated at what time point the assessment was made.

The Panel noted information from the Heart Protection Study (1999) which was being carried out on patients who were considered to be at elevated risk of coronary heart disease death because of past history.

The Panel considered that overall the data were not sufficient to support the claim 'up to 9 out of 10 CHD patients can reach the LDL-C goal of <3mmol/l'. The Pedersen study supported the claim but only for a 40mg dose of Zocor. Data on file from the Giles study (Zocor 10mg) and the Heart Protection Study (Zocor 40mg) lacked sufficient detail to allow the clinical significance of either to be assessed. In addition the Panel considered that the claim '9 out of 10' would be read as applying to all doses of Zocor; the use of the words 'up to' were not enough to correct this misleading impression. Overall the Panel considered that the claim was misleading, exaggerated and not capable of substantiation. The Panel ruled breaches of Clauses 7.2, 7.3 and 7.8 of the Code.

The Panel considered that the lipid parameters referred to (LDL-C and total cholesterol) were not unacceptable as both were relevant. The Panel ruled no breach of Clause 7.2 of the Code in this regard.

Complaint received **6 October 1999**

Case completed **6 January 2000**

LILLY v LUNDBECK

Cipramil journal advertisement

Lilly complained about a double spread journal advertisement for Cipramil (citalopram) issued by Lundbeck. The headline was 'Cipramil delivers' followed by text comparing Cipramil favourably with fluoxetine, Lilly's product Prozac. Lilly considered the advertisement to be knocking copy as it used the same wording as in Lilly's current campaign 'Prozac delivers' and similar imagery – a man with a bunch of flowers – to that of Lilly's – a man with red roses/red balloons/red wrapped parcels – seated in the background looking dejected. Lilly referred to an earlier case involving the use of parody (Case AUTH/398/2/96). Lilly alleged that the text was also knocking, implying that citalopram delivered 'ahead of fluoxetine' and 'when fluoxetine doesn't'.

The Panel noted that in Case AUTH/398/2/96 the Appeal Board had expressed some concerns about the use of parody in pharmaceutical advertising but had stated that each case would have to be judged on its merits. The Appeal Board had upheld the Panel's ruling of no breach of the Code in that case.

The Panel noted, in the case now before it, that the Cipramil advertisement was clearly based on the 'Prozac delivers' campaign. The advertisement featured the photograph of a man with a bouquet of cream flowers. In the background, sat on a bench and out of focus, was a dejected looking man holding a bunch of red roses and some red balloons with a red parcel at his side, these items had all been prominent in the Prozac campaign.

The Panel noted the claims 'Cipramil delivers ahead of fluoxetine' and 'Cipramil delivers when fluoxetine doesn't'. Adverse comments about competitor products were not in breach of the Code *per se* providing that such critical references were accurate, balanced, fair and could be substantiated. The Panel noted that there was no allegation that the claims were inaccurate, unbalanced, unfair or could not be substantiated. Lundbeck had produced evidence to support the claims. The Panel made no ruling in this regard.

Overall the Panel did not consider that the imagery and use of parody in the Cipramil advertisement in itself disparaged Prozac. No breach of the Code was ruled.

Eli Lilly and Company Limited complained about a double page spread journal advertisement (ref 1099/CIP/501/067) for Cipramil (citalopram) issued by Lundbeck Ltd. The headline was 'Cipramil delivers' followed by text comparing Cipramil favourably with fluoxetine (Lilly's product Prozac).

COMPLAINT

Lilly alleged that the advertisement was a flagrant display of 'knocking copy' and in breach of Clause 8.1 of the Code.

The advertisement used the same wording as for Lilly's current campaign 'Prozac delivers' and similar imagery – a man with a bunch of flowers – to that of Lilly's – a man with red roses/red balloons/red wrapped parcels – seated in the background looking dejected.

The text of the advertisement taken alongside the imagery was also 'knocking' implying that citalopram delivered 'ahead of fluoxetine' and 'when fluoxetine doesn't'.

Lilly believed that precedent had been set in an Appeal Board ruling (Case AUTH/398/2/96) which involved the use of similar imagery in an advertising campaign for a product within the same therapeutic area. The ruling in that case stated 'The Appeal Board then considered in general terms the use of parody in pharmaceutical advertising whereby a company reflected in its advertising the style or theme of another company's advertising. The Appeal Board considered that it would generally be difficult for companies to keep the use of parody in advertising within the requirements of the Code. It was the Appeal Board's view that it would not be in the industry's interest for the use of parody to become widespread and could envisage such activity deteriorating into abusive exchanges between competitor companies. Each case would, however, have to be judged on its own merits.'

Lilly believed that campaigns such as this were not in the interests of the industry.

RESPONSE

Lundbeck stated that it was a little disappointed that Lilly regarded its claim that Cipramil delivers 'ahead of fluoxetine' as knocking. This issue had already been considered when Lilly complained previously (Case AUTH/796/11/98) and the Panel ruled in Lundbeck's favour, a ruling which was upheld on appeal. Lilly provided no new data to change this claim and Lundbeck was unaware that the facts quoted had changed. If the facts were acceptable in July 1999, they were not 'knocking' now.

With regard to the second point, Cipramil delivers 'when fluoxetine doesn't,' Lundbeck provided a poster from the American Psychiatric Association meeting in May 1999. The study described 57 patients who had not responded to a minimum six week treatment period with fluoxetine. All subjects were switched to Cipramil and significant improvements in Hamilton Depression Rating Scale were observed from the end of the first week of treatment. Clinical Global Impression scores and Hamilton anxiety scores were also significantly improved compared to the scores whilst on fluoxetine. Since the poster was presented at a public meeting and was widely available for review, it was Lundbeck's contention that the facts contained within it withstood critical scrutiny.

Lundbeck submitted, therefore, that since neither of the claims made in favour of Cipramil versus

fluoxetine were incorrect, use of the statements 'ahead of fluoxetine' and 'when fluoxetine doesn't' was entirely appropriate.

Since both statements were supported by factual data, they could not be considered 'knocking' copy under Clause 8.1 of the Code. In this circumstances Lundbeck contended that there was no case for it to answer under this clause of the Code.

PANEL RULING

The Panel noted that in Case AUTH/398/2/96 the Appeal Board had expressed some concerns about the use of parody in pharmaceutical advertising but had stated that each case would have to be judged on its merits. The Appeal Board had upheld the Panel's ruling of no breach of Clause 8.1 of the Code.

The Panel noted, in the case now before it, that the Cipramil advertisement was clearly based on the 'Prozac delivers' campaign. The advertisement featured the photograph of a man with a bouquet of cream flowers. In the background, sat on a bench and out of focus, was a dejected looking man holding a bunch of red roses and some red balloons with a red parcel at his side – these items had all been prominent in the Prozac campaign.

The Panel noted the claims 'Cipramil delivers ahead of fluoxetine' and 'Cipramil delivers when fluoxetine doesn't'. Adverse comments about competitor products were not in breach of the Code *per se* providing that such critical references were accurate, balanced, fair and could be substantiated. This was reflected in the supplementary information to Clause 8.1. The Panel noted that there was no allegation that the claims were inaccurate, unbalanced, unfair or could not be substantiated. Lundbeck had produced evidence to support the claims. The Panel made no ruling in this regard.

Overall the Panel did not consider that the imagery and use of parody in the Cipramil advertisement in itself disparaged Prozac. No breach of Clause 8.1 was ruled.

Complaint received **8 October 1999**

Case completed **25 November 1999**

CASE AUTH/940/10/99

PHARMACEUTICAL ADVISER v WYETH

Etanercept – meeting and letter from representative

A health authority pharmaceutical adviser complained about a meeting which she had attended and which had been supported by an educational grant from Wyeth. The booking form/agenda stated that a series of meetings had been developed for healthcare purchasers and planners to help them make informed choices in complex areas. The first presentation in the afternoon was a case study of a new class of high cost medicine in a low priority area. The covering letter revealed that the low priority area was rheumatoid arthritis and mentioned that the new medicine was supported by excellent evidence of effectiveness.

The complainant said that the meeting did not meet the stated objectives and was, she believed, designed solely to promote etanercept, a Wyeth product not yet licensed. The information provided was not balanced and no opportunity had been given to question its validity. The complainant believed that the meeting was purely promotional in nature but disguised as an academic forum. The complainant also referred to a letter and journal reprint relating to etanercept which she had received from a Wyeth representative.

The Panel noted that etanercept was an unlicensed medicine. The Code prohibited the promotion of a medicine prior to the grant of a marketing authorization but the supplementary information provided a limited exemption to that prohibition and permitted companies to provide health authorities and trust hospitals etc with advance information about the introduction of new medicines which might significantly affect their levels of expenditure. The information must relate to, *inter alia*, a product which contained a new active substance and be directed to those responsible for making policy decisions on budgets rather than those expected to prescribe. The likely cost and budgetary implications must be indicated and must be such that they would make significant differences in expenditure.

In relation to the letter, the Panel noted that it requested an appointment to discuss 'a new breakthrough' in the treatment of rheumatoid arthritis. In the Panel's view this was a promotional claim and in that regard set the wrong tone for the rest of the letter. The impression was that the discussion would be about the product and not about the significant budgetary implications of its introduction. In addition, a 22 page published review of etanercept had been sent with the letter which the Panel considered was more than the 'succinct account of the product's properties' which was allowed. In the Panel's view the letter promoted etanercept prior to the grant of its marketing authorization and a breach of the Code was ruled.

In relation to the meeting, the Panel's view was that the case study did not meet the requirements for advance notification. The case study had been presented at a meeting about setting priorities in the NHS sponsored by Wyeth. The meeting had not been described as providing advance notification about the introduction of a new medicine. The Panel queried whether the intended audience, directors and consultants in public health, clinical directors, medical and pharmaceutical advisers and primary care group chief executives, were all responsible for making policy decisions on budgets, rather than those expected to prescribe as was required. The Panel also queried whether the information provided in the case study, and the description that the medicine was supported by excellent evidence of effectiveness, met the requirement that only factual information limited to that sufficient to provide an adequate but succinct account of the product must be provided. Overall the Panel considered that the arrangements were such that the presentation was disguised promotion of etanercept prior to the grant of its marketing authorization. Breaches of the Code were ruled.

A health authority pharmaceutical adviser complained about a one day meeting for healthcare commissioners, providers and planners organised by a health service organisation which had been supported by an educational grant from Wyeth. The booking form/agenda stated that a series of meetings had been developed specifically for healthcare purchasers and planners to provide help in making informed choices in complex areas. The meetings would offer the opportunity to consider ideas for a framework for priority setting and to discuss experiences in different areas. The first session in the afternoon was the presentation of a case study of a new class of high cost medicine in a low priority area. A covering letter, on the headed paper of a university and the health service organisation, revealed that the low priority disease area was rheumatoid arthritis and mentioned that the new medicine was supported by excellent evidence of effectiveness. Both the booking form/agenda and the covering letter stated that the meetings were being supported by an educational grant from Wyeth.

The pharmaceutical adviser also complained about a letter which she had received from a Wyeth representative which referred to Enbrel (etanercept), an as yet unlicensed product for the treatment of rheumatoid arthritis. The letter enclosed an ADIS reprint from Drugs 1999 entitled 'Etanercept. A review of its use in rheumatoid arthritis'.

COMPLAINT

The complainant stated that she was concerned about the activities of Wyeth. In particular, her concerns were:

- the meeting did not meet the stated objectives;
- the meeting was, she believed, designed solely to promote etanercept;
- etanercept did not yet have a product licence;
- the information provided was not balanced, and no opportunity was given to question its validity or accuracy;
- the complainant believed the meeting was purely

promotional in nature but disguised as an academic forum.

In a letter which the complainant had written to the health service organisation, a copy of which was provided, the complainant stated that she had been most disappointed with the event which had promised to be a stimulating and interesting academic debate about priority setting in the NHS. She was careful to choose which meetings to attend and avoided those that were essentially promotional in nature. The complainant had been alarmed, when people introduced themselves, how many delegates were Wyeth employees. One of the presentations had been blatantly promotional for etanercept. There had been no balance to the debate. Delegates were not given the opportunity to assess original trial evidence and thus the presentation consisted entirely of the presenter's personal opinion. The complainant considered that the meeting essentially had two goals; promoting etanercept and raising awareness of rheumatoid arthritis. It was the complainant's opinion that the stated objectives of the meeting were not met. The complainant had left the meeting before the end.

On a separate but related note the complainant stated that, the day before the meeting, she had received a letter and journal re-print which referred to etanercept.

When writing to Wyeth, the Authority drew attention to Clauses 3.1, 7.2, 9.1 and 10.1 of the Code in relation to the meeting and to Clause 3.1 in relation to the letter.

RESPONSE

Wyeth responded separately in relation to the meeting and the letter.

1 Letter from representative

Wyeth stated that the letter had been sent to healthcare purchasers ie directors and consultants in public health, clinical directors, medical and pharmaceutical advisers and primary care group (PCG) chief executives. A third party supplied the names and addresses.

The letter contained: background data on the economics associated with rheumatoid arthritis, essential in gaining a clear perspective on the budgetary implications associated with etanercept; an explanation regarding the role of tumour necrosis factor alpha in rheumatoid arthritis such that it was then possible to understand what etanercept was; a reference to the licence submission and trade-name; a statement regarding the clinical summary provided in the enclosed ADIS review and clear indication of the potential budgetary implications of the product.

The ADIS reprint was enclosed with the letter as a means of summarising the clinical information available on the product, thereby providing an adequate but succinct account of the product's properties. The publication was also independent and peer reviewed.

Wyeth submitted that the letter and its enclosures were informational and not promotional, and satisfied the criteria set out in the supplementary information to Clause 3.1 of the Code. In Wyeth's view they did not breach Clause 3.1.

2 Meetings

2.1 Meeting format and Wyeth involvement

Wyeth stated that the meeting concept originated from a discussion between Wyeth and the health service organisation in question. The discussion concerned the variations that existed within core healthcare services, and approaches to high efficacy, high cost products in a low priority area – it was agreed that rheumatology was an appropriate example of such concerns.

The discussion then went on to look at healthcare purchasers' attitudes to such a low priority area, and the need for a clear baseline to be established. This was achieved via a survey which assessed the extent to which purchasers understood the local burden of rheumatoid arthritis; the extent to which best practice was currently in place; examples of best practice and barriers to the understanding of best practice.

Wyeth had no involvement in the content of the survey.

A third party researched the outline agenda of the meetings with its target audience (healthcare purchasers) before being adapted and the new format agreed with the health service organisation. The speakers were selected and agreed upon primarily by the health service organisation, Wyeth did not select or brief the speakers and facilitators, although it did suggest one suitable speaker. The meeting venues were chosen to achieve a geographical spread, and the dates were chosen by the health service organisation.

An example of the brief given to both the facilitators and the speakers was provided.

The delegates were directors and consultants in public health, clinical directors, medical and pharmaceutical advisers and chief executives of primary care groups.

One or more representatives from Wyeth attended each meeting, but they did not actively participate in any way. At the meeting in question there were four Wyeth attendees, all were there as observers. Wyeth stressed that they did not participate in any way and did not attend the workshops.

Meetings had been held in Bristol, Stratford, Manchester and York. The remaining meetings scheduled on the original programme were cancelled some time ago.

Wyeth's financial involvement with the meetings was £8,000 per meeting, including all the speakers' honoraria.

One off costs of £40,000 were also incurred in the development and utilisation of the purchaser survey, and the development and mailing of the meeting agenda.

2.2 Concerns raised by the complainant

The meeting did not meet the stated objectives

Wyeth stated that the meeting sessions were designed to allow healthcare purchasers the opportunity to: discuss/familiarise/question the priority setting framework; gain an understanding of the lack of uniform strategy in low priority areas, using rheumatoid arthritis as an example; listen to a presentation regarding a new high cost medicine in a low priority area, such as rheumatoid arthritis; test the priority setting framework in the context of a new high cost medicine in a low priority area, and evaluate the budgetary implications associated with such a medicine.

To allow these objectives to be reached attendance at the entire meeting would be required.

Wyeth noted that the complainant left the meeting before its conclusion, and was not present for the second series of workshops following the case study presentation. Under those circumstances Wyeth suggested that it was difficult for her to comment on whether or not the meeting objectives were achieved.

Feedback forms completed after the meetings clearly showed that the complainant's view was unrepresentative of the group as a whole, indeed the health service organisation had received letters praising the meeting, one of which cited the entire meeting programme as being '… well balanced'.

The meeting was designed solely to promote the new medicine, but disguised as an academic forum

Wyeth strongly refuted the suggestion that these meetings were designed as a means of promoting etanercept. The product did not yet have a marketing authorization and Wyeth was well aware that promotion would contravene the Code and the law.

The mailing letter and accompanying agenda clearly stated that the meeting was being supported by an educational grant from Wyeth Laboratories. The letter also clearly stated that a case study would be presented to test priority setting frameworks, and that this case study involved an expensive new medicine supported by evidence of effectiveness in a low priority disease area ie rheumatoid arthritis.

The survey accompanying the mailing letter also clearly referred to the area of rheumatology, and the intention to present the results of this survey at the meetings.

Given that the complainant would have received, from the National Prescribing Centre, a copy of its monograph on etanercept, and would also have seen the letter from Wyeth's representative prior to attending the meeting, Wyeth believed that it was wrong for her to suggest that any element of disguise had been employed. The purpose of the meeting and Wyeth's connection with it were publicised appropriately.

Information presented was not balanced, and no opportunity was given to question its validity or accuracy

The presentation in question was given in the form of a case study, and was intended to stimulate a discussion on the possible budgetary implications of an expensive new medicine in a low priority disease area. It was balanced and factual in content, and was discussed in the workshops that followed.

Unfortunately the complainant left the meeting prior to the commencement of these workshops.

Supplementary information to Clause 3.1 stated that any product information provided should be:

'… limited to that sufficient to provide an adequate but succinct account of the product's properties: other products should only be mentioned to put the new product into context in the therapeutic area concerned'.

Etanercept was one of new class of medicines and as such the only comparative data available was with placebo. This meant that the only realistic means of providing an overview of its efficacy in rheumatoid arthritis was to look at response rates in terms of functional status; such information was vital if an understanding of the medicine and its possible place in therapy was to be reached.

The presentation then went on to discuss the possible budgetary implications associated with etanercept, and looked at the number of patients for whom etanercept might be useful, the impact of these patient numbers within an average health authority and the economic impact of this in terms of medicine costs and patient monitoring.

Again it was Wyeth's view that this meeting satisfied the criteria set out in the supplementary information to Clause 3.1 and, being non-promotional, did not breach that clause. Furthermore all information provided was accurate, balanced, fair, objective and unambiguous, of a high standard and provided as part of a programme which was appropriately publicised in advance.

In conclusion Wyeth did not believe that there had been breaches of Clauses 7.2, 9.1 and 10.1 of the Code.

PANEL RULING

The Panel noted that etanercept was an unlicensed medicine. Clause 3.1 of the Code prohibited the promotion of a medicine prior to the grant of a marketing authorization and reflected the legal requirements in the UK. The supplementary information to Clause 3.1, however, provided a limited exemption to that prohibition and permitted companies to provide health authorities and trust hospitals etc with advance information about the introduction of new medicines which might significantly affect their levels of expenditure. The information must relate *inter alia* to a product which contained a new active substance and be directed to those responsible for making policy decisions on budgets rather than those expected to prescribe. The likely cost and budgetary implications must be indicated and must be such that they would make significant differences to the likely expenditure of health authorities and trust hospitals and the like. Only factual information must be provided which should be limited to that sufficient to provide an adequate but succinct account of the product's properties. The information should not be in the style of promotional material and should not include mock up drafts of summaries of product characteristics. If requested further information could be supplied or a presentation made.

The Panel noted that etanercept would cost approximately £7,500 per patient per annum. There was no mention of the cost of treating patients with existing therapies. Etanercept had been used in clinical trials in patients with treatment resistant rheumatoid arthritis who had failed to respond to as many as four disease modifying anti-rheumatic drugs (DMARDs).

The Panel considered the letter from the representative and the meeting separately.

1 Letter from representative

The Panel noted that in the first paragraph of the letter the writer introduced himself as an Immunology Sales Specialist for Wyeth Laboratories and requested an appointment to discuss with the complainant 'a new breakthrough' in the treatment of rheumatoid arthritis. The letter went on to describe the clinical and economic burden of rheumatoid arthritis as well as its aetiology. Etanercept was introduced as a new therapy option that had been used in patients with treatment resistant disease. An enclosed Adis Drug Evaluation report reviewed the clinical information about the product. The letter gave details about the number of patients who might be suitable for etanercept treatment together with the estimated cost per patient per year. The letter ended by stating that Wyeth had developed a number of tools to determine the budgetary implications of etanercept on a local population and that the writer would welcome the opportunity to discuss these with the complainant.

The Panel noted that although the letter ended with a request to discuss the budgetary implications of etanercept therapy, as allowed for by the relevant supplementary information to Clause 3.2, it had opened with the description of etanercept as 'a new breakthrough' in the treatment of rheumatoid arthritis. In the Panel's view this was a promotional claim for the product and in that regard set the wrong tone for the rest of the letter. The impression was that the discussion would be about the product and not about the significant budgetary implication of its introduction. In addition, a 22 page published review of etanercept had been sent with the letter which the Panel considered was more than the 'succinct account of the product's properties' allowed for in point iv of the supplementary information. On balance the Panel considered that the letter provided information which went beyond that which was allowed by the supplementary information to Clause 3.1. In the Panel's view the letter promoted etanercept prior to the grant of its marketing authorization and a breach of Clause 3.1 was ruled.

2 Meeting

The Panel noted that it was clear both from a letter of invitation from the health service organisation, and from the booking form/agenda, that the meeting was sponsored by Wyeth. The documents stated that the meeting was about setting priorities in the NHS as due to an increase in accountability and clinical governance there was a need for healthcare commissioners, providers and planners to be more explicit about what they were going to do, or not going to do, in a cash limited world. Although, therefore, not a clinical meeting, the letter of invitation did state that a case study, which involved an expensive new medicine supported by excellent evidence of effectiveness for rheumatoid arthritis, would be used to test priority frameworks. The invitation was accompanied by a letter requesting that a survey on the provision of services for rheumatoid arthritis be completed. The letter referred to a number of new therapies to be introduced and that if this were done in an uncontrolled fashion there was a possibility that they could significantly increase costs. The letter stated that the survey was devised to collect the views and opinions of healthcare purchasers to better define the current organisation of rheumatology services in the UK. The results would be used to produce a report which would be made available on request by contributors and presented at the meeting.

The Panel did not accept Wyeth's submission that as the complainant would have received a copy of the National Prescribing Centre's monograph and the letter from the representative described in point 1 above prior to attending the meeting, it was wrong for her to suggest there was any element of disguise employed. The Panel noted that the letter from the representative to the complainant made no mention of the meeting or of setting priorities in the NHS.

The complainant stated that she had left the meeting before the final workshop sessions of the day. The complainant had, however, been present for the case study presentation. The case study was listed on the programme as a case study of a new class of high cost drug in a low priority area. The Panel noted that it had been provided with two different copies of the slides from the 45 minute case study presentation. Although the copy provided by Wyeth contained 5 more slides than that provided by the complainant, the difference was not such as to materially alter the presentation. The title slide of the case study was 'Etanercept in Rheumatoid Arthritis'. The presentation began by detailing the clinical and economic burden of rheumatoid arthritis as well as its current treatment. The second half of the presentation, however, referred to etanercept, its mode of action, suitable patients for treatment and clinical effectiveness.

The Panel noted that as etanercept was unlicensed Wyeth could not promote the product. Wyeth could provide advance notification as described in the supplementary information to Clause 3.1. In the Panel's view, however, the case study did not meet the requirements for advance notification. The case study had been presented at a meeting about setting priorities in the NHS sponsored by Wyeth. The meeting had not been described as providing advance notification about the introduction of a new medicine. The Panel queried whether the intended audience, directors and consultants in public health, clinical directors, medical and pharmaceutical advisers and primary care group chief executives were all responsible for making policy decisions on budgets rather than those expected to prescribe as required by the relevant supplementary information. The Panel also queried whether the information provided in the

case study and the description that the medicine was supported by excellent evidence of effectiveness met the requirement that only factual information limited to that sufficient to provide an adequate but succinct account of the product must be provided.

Overall the Panel considered that the arrangements were such that the presentation was disguised promotion of etanercept prior to the grant of its marketing authorization. Breaches of Clause 3.1 and of Clause 10.1 were ruled.

The Panel noted that there was an allegation that the information presented was not balanced. The Panel did not know whether or not this was so. Bearing in mind that it had already ruled breaches of Clauses 3.1 and 10.1 there was no need to consider whether or not the information was balanced. The Panel therefore decided that its rulings of breaches of Clauses 3.1 and 10.1 covered the consideration of a breach of Clause 7.2.

The Panel considered that its ruling of breaches of Clauses 3.1 and 10.1 covered the consideration of a breach of Clause 9.1.

Complaint received **12 October 1999**

Case completed **6 December 1999**

CASE AUTH/941/10/99

HOSPITAL CONSULTANT v MERCK SHARP & DOHME

Zocor letter

A consultant lipidologist complained about a 'Dear Doctor' letter announcing a price reduction across all doses of Zocor, one of Merck Sharp & Dohme's products. The letter stated that Zocor could deliver up to 9 out of 10 patients to target cholesterol levels and that many would achieve target levels using a dose of 10mg. The letter also stated that Zocor offered unique benefits to the NHS and patients through its unsurpassed survival data, efficacy across all lipid parameters, proven long term tolerability and cost effectiveness data.

The complainant alleged that the letter was misleading. Zocor was neither unique nor unsurpassed regarding the stated benefits. Patients on 10mg or 20mg would not achieve the target levels in the proportion mentioned in the letter. The Panel considered that the word unique was used to imply a general superiority and that unsurpassed would be taken to apply to all the benefits listed. The Panel considered that the claim was misleading and implied a special merit that could not be substantiated. Breaches of the Code were ruled. The Panel considered that its rulings of breaches of the Code in Case AUTH/937/10/99 with regard to the claim 'up to 9 out of 10 CHD patients can reach the LDL-C goal of <3mmol' also applied here.

A consultant lipidologist complained about a letter received from Merck Sharp & Dohme Limited which announced a price reduction across all doses of Zocor (simvastatin) (ref. 10-00 ZCR.99.GB.10333.7m.QO.1099). In addition to price information the letter detailed the clinical efficacy of Zocor. The letter stated that 'Zocor can deliver up to 9 out of 10 patients to the target cholesterol levels outlined in the new Joint British Recommendations for Coronary Heart Disease and many patients will achieve target levels using the 10mg starting dose'. It also was stated that 'Zocor offers unique benefits to the NHS and patients through its unsurpassed survival data, efficacy across all lipid parameters, proven long-term tolerability and cost-effectiveness data'.

COMPLAINT

The complainant stated that the letter was misleading and a misrepresentation of the facts. In his experience Zocor was neither unique nor was it unsurpassed regarding the benefits detailed in the letter.

The complainant stated that whilst most clinicians welcomed the consensus achieved in the Joint British Recommendation for Coronary Heart Disease, patients on 10mg or 20mg Zocor would not achieve these target levels in the proportion mentioned in the letter.

RESPONSE

Merck Sharp & Dohme submitted that with regard to the overall benefits of Zocor the complainant had misread the letter. The claim in question made it quite clear that Zocor offered unique benefits to the NHS which were then documented. The complainant seemed to have misinterpreted the word 'unsurpassed' which had to be read in the context of the sentence which read 'unsurpassed survival data'. Merck Sharp & Dohme stated that the 4S Study had yet to be surpassed by any other study in lipid lowering.

Merck Sharp & Dohme stated that the letter clearly stated that 'Zocor can deliver up to 9 out of 10 patients to the target cholesterol levels outlined in the new Joint British Recommendations for Coronary Heart Disease and many patients will achieve target levels using the 10mg starting dose'. The company did not state that all patients on any dose of Zocor would achieve this target. Data was provided to show that over 70% of patients could achieve this target level using the 10mg starting dose.

PANEL RULING

The Panel considered that the sentence 'Zocor offers unique benefits to the NHS and patients through its unsurpassed survival data, efficacy across all lipid parameters, proven long term tolerability and cost effectiveness data' was ambiguous and could be read as the word unsurpassed applying to all the benefits listed and not only to the survival data as submitted by Merck Sharp & Dohme. The Panel noted the supplementary information to Clause 7.8 which stated that great care needed to be taken with the use of the word unique. It might be used to describe some clearly defined special feature of a medicine. Its use to imply a general superiority was not possible to substantiate.

The Panel considered that the word unique was used to imply a general superiority and that the word unsurpassed would be taken as applying to all the benefits listed. The Panel considered, therefore, that the claim was misleading and implied that Zocor had some special merit which could not be substantiated. Breaches of Clauses 7.2 and 7.8 were ruled.

The Panel noted that the claim 'Zocor can deliver up to 9 out of 10 patients to the target cholesterol levels outlined in the new Joint British Guidelines for Coronary Heart Disease and many patients will achieve target levels using the 10mg starting dose' was similar to one at issue in a previous case (Case AUTH/937/10/99).

In the previous case, Merck Sharp & Dohme provided data to support the claim. Pedersen *et al* (1999) was an abstract reporting a study carried out in patients with acute myocardial infarction (n=112) or unstable angina (n=39) and LDL-C ≥3mmol/l who were allocated to one of two strategies of lipid intervention. Both groups had dietary counselling, one group received simvastatin 40mg daily from the day of randomisation while the other started simvastatin after 3 months if LDL-C was still ≥3mmol/l. At six months 82% of patients in the deferred treatment group had reached target. 90% of patients in the immediate treatment group had reached target after 3 months and remained on target at six months.

A study by Giles *et al* (1998) showed that 83% of post myocardial infarct patients achieved a total cholesterol of less than 5.2mmol/l. The mean total cholesterol at entry was 5.97mmol/l. The choice of lipid lowering medication depended on the triglyceride level but in practice the overwhelming majority of patients were treated with simvastatin at a dose of 10mg daily. Merck Sharp & Dohme had undertaken a subgroup analysis of 229 patients who had been so treated. This analysis was presented as data on file and showed that 10mg of simvastatin achieved the stated LDL-C target of 3mmol/l in 75% of patients and total cholesterol target of 5mmol/l in 72% of patients. It was not stated what sub-group had been analysed or how it had been identified. Nor was it stated at what time point the assessment was made.

The Panel noted the information from the Heart Protection Study (1999) which was being carried out on patients who were considered to be at elevated risk of coronary heart disease death because of past history.

The Panel considered that overall the data were not sufficient to support the claim 'up to 9 out of 10 CHD patients can reach the LDL-C goal of <3mmol/l'. The Pedersen study supported the claim but only for a 40mg dose of Zocor. Data on file from the Giles study (Zocor 10mg) and the Heart Protection Study (Zocor 40mg) lacked sufficient detail to allow the clinical significance of either to be assessed. In addition the Panel considered that the claim '9 out of 10' would be read as applying to all doses of Zocor; the use of the words 'up to' were not enough to correct this misleading impression. Overall the Panel considered that the claim was misleading, exaggerated and not capable of substantiation. The Panel ruled breaches of Clauses 7.2, 7.3 and 7.8 of the Code.

The Panel decided that its rulings of breaches of Clauses 7.2, 7.3 and 7.8 in Case AUTH/937/10/99 would also apply here.

Complaint received **13 October 1999**

Case completed **6 January 2000**

CASE AUTH/942/10/99

PHARMACIST v FERRING

Testoderm leaflet

A pharmacist complained that a leaflet for Testoderm, issued by Ferring, used the display of naked people for the purpose of attracting attention. Testoderm was a transdermal patch containing testosterone, which was to be applied to the scrotal skin. The front cover of the leaflet was a photograph of a naked woman standing with her arms around a man who was in front of her. The man, who was also naked, stood with his hands on his hips. The couple appeared happy and relaxed. A piece of paper was fixed along its top edge to cover the man from his waist to his knees. The piece of paper stated 'doesn't he wear it well?' Lifting the piece of paper revealed a strategically placed fig leaf. The leaflet had been mailed to pharmacists.

The Panel accepted that the photograph of the naked man covered with a fig leaf and a piece of paper had some relevance to the use of Testoderm. It was important, given the existence of body patches, that prescribers knew that Testoderm was to be applied to the shaved scrotum. However, because there was no information at all on the front cover about the product, in the Panel's view it was difficult to accept that, without reference to at least the product name, the photograph alone introduced the concept of the unique scrotal route of administration. The first reference to the product and its route of administration was on the second page of the leaflet.

The Panel considered that the use of the flap of paper to uncover the fig leaf could be seen as using sexual imagery for the purpose of attracting attention to the leaflet. A breach of the Code was ruled.

A pharmacist complained about a four page Testoderm leaflet issued by Ferring Pharmaceuticals Ltd. Testoderm was a transdermal patch containing testosterone, which was to be applied to the scrotal skin. The front cover was a photograph of a naked woman standing with her arms around a man who was standing in front of her. The man, who was also naked, stood with his hands on his hips. The couple appeared happy and relaxed. A piece of paper was fixed along its top edge to cover the man from his waist to his knees. The piece of paper stated 'doesn't he wear it well?' Lifting the piece of paper revealed a strategically placed fig leaf. The leaflet had been mailed to pharmacists.

COMPLAINT

The complainant noted that the Code stated that the display of naked or partially naked people for the purpose of attracting attention was prohibited. The complainant alleged that the leaflet breached the Code.

RESPONSE

Ferring noted that there was no allegation that the image was offensive. Clause 9.1 of the Code was pertinent to the use of this imagery. It stated that 'All material and activities must recognise the special nature of medicines and the professional standing of the audience to which they are directed and must not be likely to cause offence. High standards must be maintained at all times'. The supplementary information to Clause 9.1 stated that it would be unacceptable to use 'the display of naked or partially naked people for the purpose of attracting attention to the material or the use of sexual imagery for that purpose'.

Ferring submitted that it was important to consider the background to developing the image used.

Testosterone deficiency could cause many miserable symptoms including depression, fatigue, diminished libido, erectile dysfunction and mood swings, which were not only of significance to the affected man but also for those close to him. Unfortunately, because in general practice there was often a low awareness of this relatively uncommon but important condition and its symptoms, cases of testosterone deficiency were sometimes misdiagnosed as depression and treated inappropriately with antidepressants rather than with testosterone replacement therapy. A male patient treated for testosterone deficiency could benefit dramatically from improvements in his quality of life that would also be important in terms of the relationship with his partner.

The route of administration for Testoderm was unique in that it was a transdermal patch that was applied to the shaved scrotum. It was important to ensure that this concept was clarified so that it was completely understood before the rationale for this approach to treatment could be fully appreciated and accepted.

Current treatment options, including injections, implants, body patches and oral therapies, were not ideal. A recent Drugs and Therapeutics Bulletin discussed each of the available treatments. Of particular relevance to Testoderm scrotal patches were the known problems associated with the currently available body patches, which included a relatively high incidence of skin irritation that was sometimes very severe. Patients had also complained that the body patch was indiscreet because it was too large and that it had a tendency to rustle. Testoderm avoided the use of chemical permeability enhancers because the skin of the scrotum was thin and permeable and this resulted in a low incidence of skin irritation. The scrotal application site also meant that Testoderm was remarkably discreet.

The imagery used in the leaflet was developed and tested with the assistance of independent professionals, who represented the intended audiences including endocrinology and urology consultants and professors, general practitioners and pharmacists. The image not only drew attention to the benefits of testosterone replacement therapy but

also to the unique scrotal route of administration for Testoderm.

The image of the couple portrayed a relaxed, happy and well-balanced man with a good quality of life and a comfortable relationship with his partner, specifically avoiding any sexual overtones. This was intended to demonstrate the benefit of testosterone replacement therapy and that both the man and his partner were happy with the improved qualify of life provided by Testoderm.

The unique mode of delivery employed by Testoderm scrotal patches was also introduced in the imagery through the use of the classical fig leaf. This served the dual purposes of highlighting the application site and demonstrating that, unlike current transdermal alternatives, the patch was so discreet it would not be seen. The imagery was complemented by the phrase 'doesn't he wear it well?' which reinforced the comfortable, discreet nature of the patch, the benefits of treatment and that Testoderm was well tolerated.

Ferring submitted that the application of a patch to the skin of the scrotum was an unusual mode of delivery for a medicinal product and it was important to draw attention to this early on in the promotion of Testoderm. Some people initially found the concept of the scrotal patch difficult to accept, simply because of the application site. This imagery employed here was one way to address these initial concerns and begin serious discussions.

In summary, Ferring did not consider that there was a breach of the Code simply through the depiction of partially naked people, indeed there were examples where such images had previously been employed, particularly to illustrate transdermal therapy. There was no complaint that the material actually caused offence. The Code stated that it would be unacceptable to use the display of naked or partially naked people for the purpose of attracting attention to the material.

In this case, it was important to note the use of the image was not for the sole purpose of attracting attention to the material. The imagery, which was developed with the assistance of independent consultants from the intended professional audience, enabled the introduction of the concept of the unique scrotal route of administration employed by Testoderm. The use of the semi-naked couple was certainly not gratuitous but was fully justified and entirely appropriate to illustrate the benefits of treatment and to highlight the scrotal application site.

PANEL RULING

The Panel examined the leaflet in question. The Panel accepted that the photograph of the naked man, covered with the fig leaf and the piece of paper fixed to the mailing, had some relevance to the use of Testoderm. It was important, given the existence of a testosterone body patch, that prescribers knew that Testoderm was to be applied to the shaved scrotum. There was no information on the front cover about the product or its application. The front cover consisted only of the photograph with the piece of paper and the statement 'doesn't he wear it well?' Because there was no information at all on the front cover about the product, in the Panel's view it was difficult to accept Ferring's submission that the photograph alone introduced the concept of the unique scrotal route of administration without reference to at least the product name. The second page of the leaflet which included a 'Dear Pharmacist' letter was the first reference to the product and its route of administration.

The Panel noted the submission from Ferring in relation to the use of Testoderm and that testosterone deficiency could lead to diminished libido, mood swings, etc.

The Panel noted the supplementary information to Clause 9.1 which stated that certain types, styles and methods of promotion were unacceptable. These included the display of naked or partially naked people for the purpose of attracting attention or the use of sexual imagery for that purpose.

The Panel considered that the use of the flap of paper to uncover the fig leaf could be seen as using sexual imagery for the purpose of attracting attention to the leaflet. A breach of Clause 9.1 of the Code was ruled.

Complaint received **13 October 1999**

Case completed **23 November 1999**

CASE AUTH/943/10/99

NEXSTAR v WYETH

Abelcet press release

NeXstar complained about a press release from Wyeth which gave details of a new 50mg vial size of Abelcet. A pack shot and a summary of product characteristics (SPC) were sent with it. It was alleged that the claim 'Abelcet is already the most cost-effective lipid-based amphotericin B formulation …' was inaccurate and unfair and could not be substantiated as no evidence existed to demonstrate the superior cost effectiveness of Abelcet over other lipid formulations of amphotericin B. It was also alleged that prescribing information should have been included, that no clear reference had been given and that the press release was disguised promotion. NeXstar marketed AmBisome, an alternative lipid based formulation of amphotericin B.

The Panel noted that Wyeth acknowledged that the cost effectiveness claim was unacceptable. No data had been put forward to support it. It was inaccurate and unfair as alleged and not capable of substantiation. Breaches of the Code were ruled. Press releases were not required to bear prescribing information and no breach was ruled in that regard. No reference was needed as the material did not refer to a published study and no breach was ruled in that regard. The Panel considered that the document was clearly a press release and such documents would be promotional in the broadest sense of the word. Readers would not be misled into thinking it was anything other than a press release and no breach was ruled in that regard.

NeXstar Pharmaceuticals Ltd complained about a press release produced by Wyeth which gave details about a new 50mg vial size for Abelcet (amphotericin B lipid complex). The press release had been sent with a pack shot and a summary of product characteristics (SPC) to mainly medical and pharmaceutical journals. NeXstar marketed AmBisome, an alternative lipid based formulation of amphotericin B.

COMPLAINT

NeXstar drew attention to the claim 'Abelcet is already the most cost-effective lipid-based amphotericin B formulation...'

NeXstar alleged that the claim was promotional and therefore the press release was a promotional item. A breach of Clause 4.1 was alleged, as prescribing information did not form part of the item. A separate SPC was supplied with the mailing.

A breach of Clause 7.2 was alleged as the claim regarding the cost-effectiveness of Abelcet was inaccurate and unfair. No evidence existed to demonstrate the superior cost-effectiveness of Abelcet over other lipid formulations of amphotericin B. The only comparative study which had examined average dosage and duration of therapy with Abelcet and AmBisome was the retrospective analysis of Clark *et al* (1998), which suggested, in 59 patients undergoing 68 courses of therapy, that AmBisome at an average daily dose of approximately 2mg/kg/day for 9 days resulted in a similar outcome to Abelcet at 5mg/kg/day for 14 days. At the standard NHS price of £119 per 50mg vial, the overall treatment cost for AmBisome amounted to £3,213 for a 70kg patient. Even with the new vial size for Abelcet, the overall treatment cost with that product amounted to £4,149. Obviously, this took no account of potential savings afforded by a shorter treatment duration, such as a possibly shorter hospital stay. A breach of Clause 7.3 was alleged as the claim could not be substantiated. A breach of Clause 7.5 was also alleged as no clear reference was given.

NeXstar also alleged a breach of Clause 10.1 as the item was disguised promotion, presented as an impartial press release when it was in fact a promotional item designed to gain favourable coverage in medical journals.

NeXstar pointed out that it had recently had a complaint upheld in which a claim that Abelcet was the least expensive lipid formulation of amphotericin B had been ruled to be misleading in breach of Clause 7.2 of the Code (Case AUTH/860/3/99). The Authority noted that Case AUTH/860/3/99 had been against The Liposome Company which had formerly marketed Abelcet.

RESPONSE

Wyeth stated that it was responsible for the sales and marketing of Abelcet, whilst The Liposome Company remained the marketing authorization holder.

Wyeth stated that The Liposome Company had not informed Wyeth of the ruling in Case AUTH/860/3/99 and it only became aware of it when The Liposome Company reviewed new campaign material on Wyeth's behalf. Unfortunately Wyeth had issued the press release in question as this review was occurring.

Wyeth fully accepted that the phrase 'Abelcet is already the most cost-effective lipid based amphotericin B formulation …' was unacceptable.

PANEL RULING

The Panel noted that the press release referred only to Wyeth. There was no mention of The Liposome Company and therefore that company was not responsible under the Code.

The Panel noted that the claim at issue in Case AUTH/860/3/99 was 'Fact: Abelcet is the least expensive lipid based formulation of amphotericin B'. The claim had been ruled in breach of Clause 7.2 of the Code as Abelcet was not always the least expensive lipid based formulation of amphotericin B.

The Panel considered that the claim now at issue 'Abelcet is already the most cost-effective lipid-based

amphotericin B formulation…', was not the same as that at issue in the previous case. 'Least expensive' related only to the purchase cost of a medicine whereas 'cost-effective' included consideration of relative efficacy and incidence of side-effects etc as well as the purchase cost.

The Panel noted that Wyeth acknowledged that the claim was unacceptable. No data had been provided to support the claim. The Panel therefore ruled that the claim was inaccurate and unfair as alleged and not capable of substantiation. The Panel ruled breaches of Clauses 7.2 and 7.3 of the Code.

The Panel noted that the material at issue was a press release. In the Panel's view press releases were not required to include prescribing information as part of the document, unlike other promotional material such as journal advertising which was required to include prescribing information. Companies would be well advised to include data sheets or SPCs with press releases but there was no requirement to do so. The Panel did not accept that the press release required prescribing information printed on it as alleged and no breach of Clause 4.1 was ruled.

The claim was not one that needed to be referenced, as the material did not refer to a published study. The Panel therefore ruled no breach of Clause 7.5.

With regard to the allegation that the press release was disguised promotion the Panel noted that the document was headed 'News Release New 50mg vial size for Abelcet'. In the Panel's view the document was clearly a press release announcing the introduction of the new vial size. It did not appear to be anything other than a press release. Such items would be promotional in the broadest sense of the word. In the Panel's view readers of the material would not be misled into thinking that it was anything other than a press release. The content had been covered by the ruling of Clause 7.2. The Panel ruled no breach of Clause 10.1.

Complaint received **13 October 1999**

Case completed **6 December 1999**

CASE AUTH/944/10/99

CONSULTANT PHYSICIAN v JANSSEN-CILAG

Payment for meeting

A consultant physician complained about a letter he had received from Janssen-Cilag inviting him to a workshop entitled 'Practicalities in Managing a Hospital and Community Foot Care Service'. The letter stated that this would be comprised of a small group of regional diabetologists together with a vascular surgeon and a podiatrist; about 8-10 in all. The objectives of the meeting were to outline some of the issues and problems that faced clinicians in managing a foot care service, to share problems and develop solutions, to present the latest clinical data on Regranex (becaplermin), a Janssen-Cilag product, discuss issues in its potential clinical uptake and to identify any regional 'educational' initiatives that Janssen-Cilag might support. The meeting, to be held in a hotel, would start with an informal dinner on the first evening and finish with a buffet lunch the next day. Delegates would be expected to stay overnight so as to have an opportunity for informal discussions about some of the issues. Delegates were offered an honorarium of £350 for their time in participating in the meeting together with reasonable travel and accommodation expenses. The complainant was concerned that an honorarium was being offered purely to attend the meeting, and questioned whether this was within the Code.

The Panel noted that it had been established that in principle it was acceptable for companies to pay healthcare professionals for advice as to how their products should be promoted. There was a difference between holding a meeting for health professionals and employing them to act as consultants. In the case now before it the Panel noted that there had been seven workshops, covering England, Scotland and Wales with few company personnel at each. In the Panel's view, the lack of national guidelines and the variation in treatment protocols, even within regions, was sufficient justification for the number of meetings held. Although at each meeting there had been a presentation on Regranex, this was short in comparison to the length of the meetings, and the Panel considered that given the purpose of the meetings, such a presentation was inevitable. The Panel considered that inviting only 8-10 delegates ensured that each could make a contribution to the proceedings. The Panel had some concerns but decided that on balance the company was in effect employing the health professionals to act as consultants. In that regard the Panel accepted that the payment of an honorarium of £350 was a genuine payment for advice. Although on the borderline it was not unreasonable for the amount of work involved. The Panel therefore ruled no breach of the Code in that respect.

The Panel noted that the letter of invitation made no mention that the recipient was being invited to the workshop to act as a consultant to Janssen-Cilag. The letter referred to a presentation on Regranex. The objectives of the meeting were described as threefold. The presentation on Regranex was afforded equal prominence to the other two objectives. Although the letter referred to an honorarium of £350 'for your time in participating in the meeting' it appeared that the meeting was a promotional meeting on Regranex. The Panel fully understood the concerns of the complainant, as the failure to explain in the letter of invitation that delegates were expected to actively contribute their expertise to the meeting and were, in effect, acting as consultants to the company, meant that the impression was given that the payment was to be made for attending a promotional meeting. The Panel considered that this meant that the company had failed to maintain a high standard of ethical conduct and a breach of the Code was ruled in that regard.

A consultant physician complained about the arrangements for a meeting organised by Janssen-Cilag Ltd. The letter of invitation stated that the workshop, 'Practicalities in Managing a Hospital and Community Foot Care Service', would comprise a small group of regional diabetologists together with a vascular surgeon and a senior podiatrist. In all there would be 8-10 delegates. The objectives of the meeting were to outline some of the issues and problems that faced clinicians in managing a foot care service – to share problems and develop solutions; to present the latest clinical data on Regranex (becaplermin), and discuss issues in its potential clinical uptake, and to identify any regional 'educational' initiatives that Janssen-Cilag might support through either financial sponsorship or other routes.

The letter stated that the meeting, to be held in a hotel, would start with an informal dinner on the first evening and finish with a buffet lunch the next day. Delegates would be expected to stay overnight so as to have an opportunity for informal discussions about some of the issues. Delegates were offered an honorarium of £350 for their time in participating in the meeting together with reasonable travel and accommodation expenses.

COMPLAINT

The complainant was concerned that an honorarium of £350, purely to attend the meeting, was being offered and questioned whether this was within the Code.

RESPONSE

Janssen-Cilag stated that in March 1999 it was granted an EU licence for Regranex (becaplermin) for the treatment of full thickness, neuropathic, chronic diabetic ulcers less than or equal to 5cm^2. Regranex was launched in the UK in mid September. It was the first prescription only medicine (POM) to be licensed in this area (all other therapies to date fell into the category of a bandage or a medical device), and contained a platelet-derived growth factor which was the product of DNA technology.

Janssen-Cilag had a general lack of knowledge in the disease area (it had no other products in the diabetes

field) and, in particular, a lack of information as to how diabetic foot ulcer patients were treated across the UK. There were no national guidelines for the management of patients with diabetic foot ulceration. It was, however, clear that the standards of care and issues associated with foot ulcer treatment (diabetic and otherwise) were extremely varied across the country. Centres of excellence were found to be few and treatment protocols (where they even existed) varied across primary/secondary care and even within localities.

The company needed to be better informed as to the diabetic foot ulcer (DFU) disease area. This included, *inter alia*, gathering information on such general topics as guidelines, audit, the healthcare economics of the diabetic foot, etc; it also included becoming better acquainted with such regional/local considerations as the practicalities of getting the product onto hospital formularies and those of primary care groups (PCGs) and identifying the proper budget holders for such a medicine. The company was also concerned about the development of next year's educational initiatives.

In conjunction with an external consultancy agency, it was decided that a group of 7 exploratory workshops would be held in different regions across the UK. The objective would be to discuss regional/local treatment patterns, referral protocols and key issues that surrounded the treatment of DFUs in that particular region. The mechanism to be employed was that of an advisory workshop, a standard tool akin to a focus group, in which the participants were asked to contribute to the meeting in a consultative way. An anonymized copy of the invitation to the workshop was provided.

The meeting at issue was the last of 7 regional workshops. Each meeting endeavoured to bring together a multidisciplinary group which could act as regional consultants to Janssen-Cilag. The summation of the meetings would show the different ways in which patients were treated across the UK.

Janssen-Cilag explained that the objectives of the advisory workshop were three fold:

a) to outline some of the practical issues surrounding the provision of a diabetic foot service, to share problems and discuss how local solutions might be developed;

b) to discuss the implications of a new POM on the provision of foot services in a locality; to do this it was necessary for the product manager to present the clinical trial data on Regranex so that the delegates might all have the same level of understanding as to the particular issues faced by Janssen-Cilag in marketing the product;

c) to identify any regional educational initiatives that Janssen-Cilag could become involved in with the local diabetic foot ulcer teams; given budget limitations it was necessary to make hard decisions as to the direction of the company's medical education programme for 2000 and beyond, in terms of investment in DFU services and training.

It should be noted that the presentation by the company's education manager on the clinical trial evidence for Regranex was short in respect of the total length of the workshop and designed to set the scene for the final interactive discussion.

A possible chairperson (diabetologist) for each area was first identified by the company and then approached by the agency to see if he/she would take responsibility for meeting the objectives of the workshop.

The chairperson was given a list of all diabetologists in the region being reviewed but was relied upon to be able to proffer the names of regional vascular surgeons and podiatrists. The chairperson was then asked to select a representative group of local experts (diabetologists, vascular surgeons and podiatrists) to attend each meeting. The actual invitations were sent from Janssen-Cilag on company stationery. Each meeting was to have approximately 8-10 delegates attending, allowing full participation and discussion throughout the programme. In reality the average number of delegates at each meeting was about 7. The chairperson was also asked to suggest possible venues for the workshops.

Details of the dates and locations for the seven regional meetings were given.

Delegates were asked to attend an evening meal where, as the invitation letter made clear, they would be asked to discuss issues surrounding DFU treatment in a more informal manner than would be the case at the following morning's session.

Janssen-Cilag was represented at each meeting by its education manager, and by the business manager of the region in which the meeting was held. The managing director of the agency also attended to record the proceedings as it was considered that this would make the production of a report easier for the agency. A confidential transcript of the meeting in question was provided.

Janssen-Cilag noted that sales representatives were not present at any of the meetings, nor were they involved in the choice or selection of participants. Moreover, no materials were given out at the meetings, except that copies of the summary of product characteristics were available upon request.

All of the programmes followed a similar format of a dinner/informal focused conversation on the night prior to the formal morning session. The meeting started the night before the formal morning session since this allowed participants to travel at their leisure, and often a significant distance, to the venue; it also allowed for an early start in the morning. Starting early in the morning in turn allowed for finishing in the early afternoon, which allowed delegates to travel back outside peak travel hours: this also offered the delegates an opportunity to return to their work base, should they wish to do so or should they have a need to do so immediately after the programme ended in the early afternoon.

The meeting in question started at 9am with a presentation by the chairman on the local foot service which was then opened up to a discussion on the local issues surrounding the care of patients with DFUs. At 11am the medical education manager presented the clinical trial evidence for Regranex and opened up the data for discussion. The meeting then

looked at local solutions/educational initiatives which might be developed as a result of the initial discussions. Local initiatives for 2000 were discussed, including the training of podiatrists in debridement technique and local team workshops.

Janssen-Cilag submitted that the transcript showed that the meeting was interactive between the chairperson and the delegates, with minimal input from the company.

Each delegate received an honorarium of £350 which the company considered was reasonable for their active contribution to the meeting, ie for expert consultation; in some cases this amount had to be used to provide locum cover for the doctor so that he/she could attend the meeting.

Each chairperson received an honorarium of £750. Chairpersons were paid more than a delegate, in respect of the administrative work that they were required to undertake prior to each meeting and in respect of their chairing of the actual meeting.

Janssen-Cilag noted that the BMA had suggested that for speaking to a non-NHS group, general practitioners should be paid £100/hour. Moreover, BMA fee guidelines in 1996 stated that for participation in clinical trials a doctor was entitled to request £120/hour. Including dinner the previous evening at which issues were discussed (2 hours) and the 4 hours of expert contribution during the morning session, a payment of £350 for 6 hours equated to £58/hour for delegates, a sum not excessive in respect of the work required and in keeping with various recognised standards of payment. The chairperson's work included a greater number of hours spent in preparation for the meeting and in the more arduous task of chairing the meeting; thus, by any calculations, the £750 honorarium to the chairperson could not be said to have been excessive.

Janssen-Cilag stated that the honoraria did not constitute a gift, benefit in kind or pecuniary advantage offered or given to healthcare professionals as an inducement to prescribe, supply, administer or buy Regranex. Rather, it constituted a genuine payment for the delegate's and the chairperson's input into the discussions and for providing information on local matters of great importance to the company; it was not an inducement in disguise.

The basic per delegate cost was £140. This rate included an evening meal, overnight accommodation, breakfast, mid-morning tea and coffee and a buffet lunch. Reasonable travel expenses were also reimbursed. The company considered that the hospitality complied with the requirements of Clause 19.1 in that it was secondary to the purpose of the meeting, the level of hospitality was appropriate and not out of proportion to the occasion and the costs would not be deemed to exceed that level which the attendees would normally adopt were they paying for themselves.

Janssen-Cilag noted that the Authority had drawn its attention to two other related cases (Cases AUTH/471/10/96 and AUTH/686/3/98). In Case AUTH/471/10/96, the respondent company was found not to have breached the Code with respect to a one-off evening focus group it held for a multidisciplinary group of clinicians and pharmacists. The Panel noted as a general principle that it accepted that there was a difference between holding a meeting for health professionals and employing them to act as consultants.

Among the criteria used by the Panel to determine the outcome of the complaint were:

1 the non-promotional nature and content of the focus group
2 the level of the honorarium paid
3 the level of the hospitality arranged
4 whether product material were distributed at the meeting
5 the number of delegates present
6 the number of company personnel present
7 how the members of the focus group were chosen.

Although concerned that the potential members of the focus group had been identified by members of the company's sales force, the Panel ruled no breach of Clause 18.1 and Clause 19.1.

With regard to the meeting now in question, and the other six regional meetings, Janssen-Cilag considered that it passed all of the above tests. The meeting in question differed only from the other six in terms of point six above; as this was the last of several meetings, Janssen-Cilag had allowed a sandwich student who had worked on the project to attend as part of her training, and the agency also allowed a junior member of its staff to attend for training purposes. Thus, there were two more people present at the meeting in question than was the case for the previous meetings, although both were there as observers only and played no active part. Likewise, the Janssen-Cilag business manager for the region was present merely for the purposes of observation. Only the company's education manager for Regranex gave a presentation, while the managing director of the agency acted only to help facilitate the discussion.

Thus the participation of Janssen-Cilag or the agency was minimal; it was the healthcare professionals' views that were sought in the workshop. There was no attempt on the part of the Regranex education manager or the agency to impose any view that could be said to be promotional.

Since it was the chairperson who was responsible for the invitations which were sent out (ie the initial selection process), the company considered that the participation of the delegates should withstand scrutiny by the Panel. The actual number of delegates attending the meeting in question in addition to the chairperson, was five – 4 doctors and 1 podiatrist; this allowed for an interactive session in which the views of all of these healthcare professionals could be elicited.

Janssen-Cilag noted that in Case AUTH/686/3/98 the respondent company had organised an evening focus group so that a group of approximately ten consultant psychiatrists could discuss the future development of a type of antidepressant from a marketing perspective; the respondent company marketed a medicine in this specific category. It transpired, however, that this meeting was one of ten meetings held around the UK. The Panel calculated that a total

of about 70 delegates would have attended the meetings. An honorarium and travel expenses were paid.

The Panel had reiterated its view that it was not unacceptable for companies to pay healthcare professionals for advice as to how products should be promoted, but that a boundary had to be drawn. For the actual meeting complained of the respondent company had written to 41 psychiatrists offering places at the focus group meeting on a first-come first-serve basis; the Panel stated that it made a distinction between inviting a small number of specific healthcare professionals and inviting a relatively large number based on a indiscriminate method of targeting delegates. Moreover, in the Panel's view, it was questionable whether, as submitted by the respondent company, that all 70 of the consultant psychiatrists involved would truly have acted as consultants to the company.

In Case AUTH/686/3/98, the Panel had noted that the arrangements for each of the 10 meetings were substantially the same as those in Case AUTH/471/10/96; hence no breach was likely on these matters. Rather, the Panel stated that another element should be examined – that of the number of meetings. Without justification as to the number of meetings held, the series of meetings took on the appearance and nature of a promotion. Therefore a breach of Clause 18.1 was ruled.

Comparing Case AUTH/686/3/98 to the case in question, Janssen-Cilag stated that no breach of Clause 19.1 should be found. However, it noted that it had arranged seven meetings at various locations throughout the country.

The company noted that the total number of attendees for all of the meetings was 51 healthcare professionals (7 chairpersons and 44 delegates), substantially lower than the 70 psychiatrists which the Panel estimated had attended the series of meetings in Case AUTH/686/3/98. More to the point was the fact that, as in Case AUTH/471/10/96, the invitees were part of a multidisciplinary group of physicians/surgeons and podiatrists: all seven chairpersons were consultant diabetologists; of the delegates 29 were doctors and 15 were podiatrists. The spectrum of disciplines and hence of views made it more likely that all those chosen could truly have acted as consultants to Janssen-Cilag. The delegates in attendance had been targeted by the chairperson according to a number of criteria and not invited on an indiscriminate free-for-all and first-come first-served basis.

Additionally, unlike the respondent company in Case AUTH/686/3/98, Janssen-Cilag considered that it had supplied the justification required regarding regional variations in the field of DFUs. Such variations (due mostly to a lack of a national standard or guidelines for the care of the diabetic foot) added weight to the procedure of sampling several regions from around the country – thus requiring several meetings, but ones which could not be equated to a series of promotional meetings.

Finally, Janssen-Cilag noted that it had engaged an agency, even before the planning of these advisory groups, to produce a report on how to proceed in making a case for Regranex as the best way forward in the care of patients with DFUs and in gaining formal acceptance of the product (ie admission onto various formularies or inclusion in local/regional guidelines). The advisory groups constituted the major means by which the agency would be able to give the company guidance. Exit questionnaires were given to the participants which elicited further advice from the participants, in addition to their comments during the workshops.

Janssen-Cilag stated that all of the advisory workshops were taped. From the tapes or the transcripts it was clear that the chairpersons and the delegates were the true participants in the meeting. Janssen-Cilag or agency personnel only participated to give the product's clinical trials history and results. The healthcare professionals played a very active role in the workshops and were not just passive listeners. Janssen-Cilag considered this to be the antithesis of promotion; when the delegates speak and the company and its agency listen, this was the hallmark of the consultation.

Janssen-Cilag denied breaches of Clause 18.1 or Clause 19.1 of the Code.

PANEL RULING

The Panel noted that it had been established that in principle it was acceptable for companies to pay healthcare professionals and others for advice as to how their products should be promoted (Case AUTH/471/10/96). There was a difference between holding a meeting for health professionals and employing them to act as consultants. A breach of the Code had been ruled in Case AUTH/686/3/98, however, because the Panel considered that a series of ten meetings, to which a relatively large number of doctors had been invited on a first-come first-served basis, constituted a series of promotional meetings. It was not appropriate to pay doctors to attend such meetings. The ruling was upheld on appeal by the respondent.

Turning to the case now before it the Panel noted that there had been seven workshops with few company personnel at each. In the Panel's view, the lack of national guidelines and the variation in treatment protocols, even within regions, was sufficient justification for the number of meetings held. The seven meetings had covered England, Scotland and Wales. Although at each meeting there had been a presentation on Regranex, this was short in comparison to the length of the meetings, and the Panel considered that given the purpose of the meetings such a presentation was inevitable. The Panel considered that inviting only 8-10 delegates ensured that each could make a contribution to the proceedings.

The Panel noted that the delegates were being employed as consultants to the company and as such their inclusion in each workshop should stand up to independent scrutiny. In that regard the Panel noted that the chairperson for each meeting had been chosen by Janssen-Cilag but that the delegates had been chosen by the chairperson. In the Panel's view it

appeared that the delegates had been carefully selected according to their expertise.

The Panel considered that the hospitality offered was not unreasonable. Dinner on the first evening had been served in a private function room which in the Panel's view would have enabled the delegates to informally discuss the issues surrounding DFU treatment. The basic cost per delegate was £140 plus travel expenses which, while possibly exceeding the level that some delegates would have paid for themselves, was not unreasonable. No breach of Clause 19.1 was ruled.

The Panel had some concerns about the meeting but decided that on balance the company was in effect employing the health professionals to act as consultants. In that regard the Panel accepted that the payment of a honorarium of £350 was a genuine payment for advice. Although on the borderline it was not unreasonable for the amount of work involved. The Panel therefore ruled no breach of Clause 18.1.

The Panel noted that the letter of invitation made no mention that the recipient was being invited to the workshop to act as a consultant to Janssen-Cilag. The letter referred to a presentation on Regranex. The objectives of the meeting were described as threefold. The presentation on Regranex was afforded equal prominence to the other two objectives. Although the letter referred to an honorarium of £350 'for your time in participating in the meeting' it appeared that the meeting was a promotional meeting on Regranex. The Panel fully understood the concerns of the complainant as the failure to explain in the letter of invitation that delegates were expected to actively contribute their expertise to the meeting and were in effect acting as consultants to the company meant that the impression was given that the payment was to be made for attending a promotional meeting. The Panel considered that this meant that the company had failed to maintain a high standard of ethical conduct and a breach of Clause 9.1 of the Code was ruled. The Panel noted that it had not been suggested to Janssen-Cilag that when responding it bore in mind the requirements of Clause 9.1 but this did not preclude the Panel from making such a ruling.

Complaint received **18 October 1999**

Case completed **6 December 1999**

CASE AUTH/945/10/99

LILLY v NOVO NORDISK

Promotion of NovoRapid

Lilly complained about the promotion of NovoRapid (insulin aspart) by Novo Nordisk. There were a number of allegations about three items, a leavepiece, guidelines and a product monograph.

Lilly alleged that the use of suppressed zeros in a graph in the leavepiece and in the product monograph exaggerated the data. The Panel considered that the use of suppressed zeros exaggerated the differences in convenience and flexibility between NovoRapid and Human Actrapid. A breach of the Code was ruled. The Panel also ruled a breach of the Code as reference was made to Novo Nordisk's product Human Actrapid in both the leavepiece and the product monograph but no prescribing information for it had been given.

Lilly alleged that a graph in the leavepiece was misleading as it failed to point out that the dose of isophane insulin was 11% higher in the NovoRapid group than in the human soluble insulin group. The relevant study was of patients treated with either insulin aspart or human soluble insulin as meal-related insulin three times daily on top of a background of once or twice daily isophane insulin. The abstract stated that the improvement in the blood glucose control seen in the insulin aspart treated patients was independent of the increased dose of isophane insulin. In the Panel's view it would have been helpful to mention the increased dose. It was not misleading to have omitted it. Doctors would not expect the dose of isophane insulin to be identical in both regimens and the increased isophane dose was not sufficient to account for the improved glucose control. No breach was ruled.

The guidelines for using NovoRapid stated that the product should reduce the need for snacks and made reference to dose adjustments prior to exercise. Lilly stated that there was no clinical data to support the claims which were speculative and unsubstantiated. The Panel noted that the advice regarding snacks and exercise was based on pharmacokinetic and pharmacodynamic data. There was no clinical data. The Panel considered that it was misleading not to state the basis of the advice and a breach of the Code was ruled.

Lilly pointed out that the product monograph stated that soluble insulin worked best when given 30 minutes or more before meals. This was misleading as the Actrapid summary of product characteristics (SPC) stated '… preparations should be followed by a meal within 30 minutes of administration'. The Panel noted that the section at issue had been written by an independent expert. Novo Nordisk was however responsible. The foreword was misleading with regard to Actrapid and a breach of the Code was ruled.

Lilly alleged that a claim for post-prandial control was overstated in the product monograph. The Panel noted the claims that NovoRapid provided significantly better post-prandial glucose control than

soluble human insulin in Type 1 and Type 2 diabetes. Another claim stated that NovoRapid had clear benefits over soluble human insulin and provided improved control of post-prandial glucose levels. The Panel noted that when human soluble insulin was administered 30 minutes before a meal the effect of the two insulins were similar. When injected close to or immediately before a meal NovoRapid provided the better control. The claims had not referred to the importance of the timing of the injections and were therefore ruled to be misleading in breach of the Code.

No breach of the Code was ruled with regard to a claim that NovoRapid was well suited to the control of post-prandial glucose excursions.

Lilly drew attention to a claim for '…clear benefits over soluble insulin in terms of …hypoglycaemic events …'. There was no statistically significant data to support an overall reduction in hypoglycaemia, only major nocturnal hypoglycaemia. The statement exaggerated the data and needed to be qualified. In the Panel's view the claim implied that NovoRapid was of clear benefit with regard to all types of hypoglycaemia which was not so. The claim which was the first sentence of the summary was qualified by the sixth which stated that the risk of major nocturnal hypoglycaemia was significantly reduced by NovoRapid compared with human soluble insulin. The Panel noted that it was an accepted principle under the Code that misleading claims could not be qualified elsewhere in a piece. The first sentence of a summary gave a misleading impression as to the effect of NovoRapid on hypoglycaemia and a breach of the Code was ruled.

Lilly alleged that a claim that '…NovoRapid is likely to result in a lower risk of hypoglycaemia between meals …' was highly speculative and unsubstantiated. There was no clinical data to support this claim, which again could not be predicted from pharmacokinetic and pharmacodynamic data. The Panel noted that the statement regarding the lower risk of hypoglycaemia between meals was based on the known pharmacokinetic profile and pharmacodynamic action of NovoRapid. It was not based on clinical data. It was misleading not to state the basis of the claim and a breach was ruled.

Lilly noted that a section on use in pregnancy appeared to be promoting use of NovoRapid outside the licence. The Panel noted that the SPC stated that there was limited use of the product in pregnancy. Animal reproduction studies had not revealed any differences between NovoRapid and human insulin regarding embryotoxicity or teratogenicity. It was also stated that intensified monitoring of pregnant women with diabetes was recommended throughout pregnancy; insulin requirements usually fell in the first trimester and increased subsequently during the second and third trimesters. The Panel noted that the NovoRapid SPC did not contain any prohibition or restriction on the use of the product during pregnancy. The product monograph had expanded on the information given in the SPC but was not inconsistent with it. The Panel did not consider that the product monograph promoted NovoRapid outside the terms of its licence and ruled no breach of the Code.

Eli Lilly and Company Limited complained about the promotion of NovoRapid (insulin aspart) by Novo Nordisk Pharmaceuticals Ltd. Three promotional items were at issue, a leavepiece (ref NR-99-007), Guidelines for using NovoRapid (ref NR-99-017) and a product monograph (ref NR-99-004). Novo Nordisk stated that the first two items had been distributed by the primary and secondary care field forces and the third item by the secondary care field force.

A Leavepiece

Page 3 was headed 'NovoRapid improves and maintains long-term glycaemic control' and bore a graph comparing HbA_{1C} reduction with NovoRapid and Human Actrapid. Page 4 was headed 'NovoRapid improves quality of life of people with diabetes', a footnote indicating that this was compared to Human Actrapid. Two bar charts compared the treatment satisfaction scores as regards the convenience and flexibility of NovoRapid and Human Actrapid (Novo Nordisk's brand name for human insulin).

1 Suppressed zeros

COMPLAINT

Lilly stated that the reduction in HbA_{1C} seen with NovoRapid was small and of doubtful clinical significance. The graph on page 3 exaggerated the reduction in HbA_{1C} by the use of a suppressed zero HbA_{1C} axis. There was similar use of a suppressed zero in the bar charts on page 4 to exaggerate the data for convenience and flexibility (Clause 7.6).

RESPONSE

Novo Nordisk said that on pages 3 and 4 the graph and the bar charts referred to all had a break in their y axis clearly indicated by two parallel diagonal lines which Novo Nordisk considered did not mislead or exaggerate the results from the studies. The values were clearly marked on the y axis and in Novo Nordisk's opinion this did not constitute a breach of Clause 7.6 of the Code. It should be remembered that HbA_{1C} values of 0 did not exist and that the results of the treatment satisfaction questionnaire were highly statistically significant (p=0.00001 for both convenience and flexibility).

PANEL RULING

The Panel noted that the y axis of the graph on page 3 was labelled HbA_{1C} (%) and started at 7.4 and rose to 8.2. The Panel noted that the BNF (28 September 1999) stated that the measurement of HbA_{1C} (a specific fraction of the total glycosylated haemoglobin) provided a good indication of long-term glycaemic control. The ideal HbA_{1C} level was around 7% although this could not always be achieved, and for those on insulin there were significantly increased risks of severe hypoglycaemia.

The graph plotted 12 month glycaemic control with either NovoRapid or Human Actrapid. The graph showed that at each time point (3, 6, 9 and 12 months)

the percentage of HbA_{1C} was always statistically significantly lower in the NovoRapid-treated group; the absolute difference between the two insulins in terms of HbA_{1C} was never more than 0.3 percentage points.

The Panel noted that the NovoRapid summary of product characteristics (SPC) stated that in two long-term open label trials in patients with Type 1 diabetes comprising 1070 and 884 patients, respectively, NovoRapid reduced glycosylated haemoglobin by 0.12 percentage points and by 0.15 percentage points compared to human insulin; a difference of doubtful clinical significance.

The Panel considered that the use of a suppressed zero in the graph gave an exaggerated impression of the impact of NovoRapid on the reduction of HbA_{1C}. A breach of Clause 7.6 was ruled.

The bar charts on page four showed differences in convenience and flexibility between NovoRapid and Human Actrapid. The chart showing convenience started with a treatment satisfaction score of 4 and rose to 5.5; the chart showing flexibility started at 4.2 and rose to 5.4. Scores in both charts were in favour of NovoRapid. With regard to flexibility the score for NovoRapid was 5.3 and that for Human Actrapid was 4.7, given the suppressed zero, however, the bar for NovoRapid was twice the height of that for Human Actrapid. Although the differences were statistically significant ($p<0.00001$) the Panel considered that the suppressed zeros exaggerated the differences in convenience and flexibility seen with the two types of insulin and a breach of Clause 7.6 was ruled.

2 Prescribing information

COMPLAINT

Lilly noted that the comparator on page 3 was specifically stated to be Human Actrapid, the brand name of Novo Nordisk's soluble insulin, but no prescribing information for that product was provided (Clause 4.1).

RESPONSE

Novo Nordisk stated that prescribing information for Human Actrapid was not included because no claim was made for it, Clause 18.3 of the Code referred.

PANEL RULING

The Panel noted that Clause 18 of the Code dealt with gifts and inducements. Clause 18.2 referred to gifts in the form of promotional aids and prizes and Clause 18.3 stated the conditions under which prescribing information did not have to be included on promotional aids. Clause 18 of the Code was not relevant to printed promotional material such as leavepieces or detail aids.

The Panel noted that the leavepiece referred to Human Actrapid. Clinical data was shown for Human Actrapid and a number of comparisons made, albeit that they were in favour of NovoRapid. Novo Nordisk had used a brand name in which it had a commercial interest. In the Panel's view the leavepiece promoted Human Actrapid. As the leavepiece did not carry the prescribing information for Human Actrapid a breach of Clause 4.1 was ruled.

3 Differences in NPH (isophane insulin) dose

COMPLAINT

Lilly stated that in the study referenced beneath the graph on page 3, the original abstract from Home *et al* (1999) clearly stated that the NPH (isophane insulin) dose was 11% higher in the NovoRapid group. Even though there had been 'statistical adjustment' of the data, in an attempt to exclude an effect, Lilly strongly felt that it was misleading not to divulge this information. There had been a fundamental change in the insulin regime and an increase in the total insulin dose. Most healthcare professionals would consider this highly relevant information (Clause 7.2).

RESPONSE

Novo Nordisk stated that on page 3, the graph was clearly referenced to reference 3 and not the reference referred to in the complaint (reference 1). In the abstract mentioned (Home *et al* (1999)), the NPH dose was 11% higher in the NovoRapid treatment group as clearly stated in the abstract. Statisticians adjusted for this effect, however, and the difference remained statistically significant after adjustment. The abstract stated '… the improvement in blood glucose control was independent of the increase in basal insulin dose'. In both groups, the meal-related (soluble/rapid-acting) insulin dose remained unchanged. In the NovoRapid group, the increase in total daily insulin dose over the Actrapid group was 0.02U/kg (which equated to 1.4 units of insulin per day in a 70kg person). This increased NPH dose therefore was not sufficient to explain the lower HbA_{1C} and was not a 'fundamental change in the insulin regime'. Novo Nordisk therefore believed this was not in breach of Clause 7.2 of the Code.

PANEL RULING

The Panel noted that the graph on page 3 was referenced to reference 3 which was given as data on file. Reference 3 had not been provided. The Panel noted that the heading to the page 'NovoRapid improves and maintains long-term glycaemic control' was referenced to references 1 and 2. The statement above the graph 'In two studies totalling more than 1900 patients HbA_{1C} was reduced with NovoRapid at 6 months' was referenced to references 1 and 2 and 'This improvement was sustained for 12 months' was referenced to reference 3.

The Panel noted that Lilly had focussed its complaint on reference 1 which was cited on the page in question but not as described by Lilly. Reference 1 was taken from an abstract (Home *et al*) in which patients with Type 1 diabetes were randomised to treatment with either insulin aspart or human soluble insulin as meal-related insulin three times daily on top of a background of once or twice daily isophane insulin. The dose of isophane insulin increased by 11%

in the insulin aspart-treated patients. The abstract stated that the improvement in the blood glucose control seen in the insulin aspart-treated patients was independent of the increased dose of isophane insulin.

In the Panel's view prescribers initiating or monitoring changes in brand or type of insulin would be aware of the resultant need for a change in dosage. In this regard the Panel noted the following note in MIMS, December 1999: 'Dosage adjustments may be required during…change in species of origin, type or purity of insulin.' In addition the NovoRapid SPC stated 'Transferring a patient to a new type or brand of insulin should be done under strict medical supervision. Changes in strength, brand, type, species (animal, human, human insulin analogue) and/or method of manufacture may result in a change in dosage. Patients taking NovoRapid may require an increased number of daily injections or a change in dosage from that used with their usual insulin. If an adjustment is needed, it may occur with the first dose or during the first several weeks or months.'

The Panel considered that, while it would have been helpful if the increased dose in the isophane insulin in the insulin aspart-treated group had been mentioned on the page, it was not misleading to have omitted it. In the Panel's view the increased isophane dosage was not a fundamental change in therapy. Doctors would not expect the dose of the isophane insulin to be identical in both regimens and the increased isophane dose in the insulin aspart-treated group was not sufficient to account for the improved glucose control observed in that group. No breach of Clause 7.2 was ruled.

B Guidelines for using NovoRapid

COMPLAINT

Lilly stated that the guidelines included the statement that 'NovoRapid should reduce the need for snacks' and references to adjustments in dose prior to exercise.

Claims about these clinically important issues could not be assumed from pharmacokinetic and pharmacodynamic information. There was no clinical data to support these claims, which were both speculative and unsubstantiated (Clause 7.3).

RESPONSE

Novo Nordisk stated that guidelines were important when introducing a new therapy and because experience with NovoRapid had been limited to clinical trial situations, Novo Nordisk had to rely on the experiences of its experts using NovoRapid in these trials in addition to their experiences in clinical practice. The guidelines were not intended as claims and were advisory only, written with the knowledge of both the pharmacokinetic and pharmacodynamic properties of the agent and with the aim of helping healthcare professionals and patients to most appropriately use this new insulin. It was Novo Nordisk's considered opinion that the advice on snacking was both appropriate and responsible. A major risk of human soluble insulin was, of course, late post-meal hypoglycaemia caused by the extended 'tail' of its action. Snacking had become a necessary part of life for many people with Type 1 diabetes and Novo Nordisk considered it desirable to give patients the best possible advice.

It was known from experience with human insulin that dose reductions prior to exercise were important and although Novo Nordisk had no studies specifically examining dose reductions and exercise, on safety grounds it believed it to be responsible to remind clinicians of the need to reduce the dose of NovoRapid before exercise planned to occur within the duration of its peak action (1-3 hours). Again this recommendation was based on the known properties of NovoRapid, the experiences of Novo Nordisk's experts who had used this insulin in clinical trials and also their experiences in clinical practice.

PANEL RULING

The Panel noted that, beneath the heading 'Differences between NovoRapid and human soluble insulin', the guidelines stated, with regard to snacks, that 'NovoRapid should reduce or remove the need for many patients to snack between meals'. With regard to exercise it was stated that if the exercise was planned and within 3 hours then 'decrease the previous meal-related NovoRapid dose. Reductions of 10-30% are quite normal and greater reductions may be required for prolonged strenuous exercise.' If exercise was to occur more than 3 hours later then 'No dose adjustment is likely to be required.' The Panel noted that the advice on exercise was not inconsistent with the relevant statement in the NovoRapid SPC that 'Adjustment of dosage may also be necessary if patients undertake increased physical activity or change their usual diet. Exercise taken immediately after a meal may increase the risk of hypoglycaemia'.

The Panel noted that it was a principle under the Code that all claims in promotional material referred to the clinical situation unless it was clearly stated otherwise. The advice regarding snacks and exercise had been based on pharmacokinetic and pharmacodynamic date. There was no clinical data to support the statements. The Panel considered, therefore, that it was misleading not to state the basis of the advice and ruled a breach of Clause 7.2.

The Panel noted that Lilly had alleged a breach of Clause 7.3 but believed that the matter was more appropriately considered under Clause 7.2 of the Code.

C Product Monograph

1 Foreword

COMPLAINT

Lilly stated that the foreword written by a professor included the statement '…soluble insulin works best when given 30 minutes or more before meals…' (page 5 of the product monograph). As a statement applying to all generic soluble insulin this applied to Novo Nordisk's soluble insulin, Actrapid. This was clearly in breach of the SPC for Actrapid, which stated that:-

'Owing to their strong early effect, injections of Human Actrapid Penfil… preparations should be followed by a meal within 30 minutes of administration'.

As a direct consequence, patients could potentially suffer hypoglycaemia. There was a recent precedent for this in Case AUTH/903/7/99.

Although the statement might be the author's opinion, it appeared within a promotional item. Lilly believed that Novo Nordisk had a clear responsibility to ensure that statements prompted by it from opinion leaders, appearing within its materials, complied with the Code (Clause 7.2).

RESPONSE

Novo Nordisk stated that the foreword was from a world authority on insulin physiology and was, of course, his opinion and it would be noted that no reference was made to any specific insulin. Novo Nordisk did not think that anyone would disagree that in controlled laboratory conditions, soluble human insulin did work best when given 30 minutes or more before a meal. However this statement could not be taken in isolation since the risk of pre-meal hypoglycaemia increased if insulin was taken more than 30 minutes before a meal. The SPC for Actrapid, which stated that '…preparations should be followed by a meal within 30 minutes of administration', reflected a balance between pragmatism and optimal effect. It would clearly be impractical (and possibly unsafe) to recommend that patients took their insulin more than 30 minutes before a meal, especially when the evidence suggested that the majority had difficulty even waiting up to 30 minutes before injection. However when designing its trials Novo Nordisk wanted to compare the best use of human soluble insulin against NovoRapid - otherwise any apparent superiority could have been attributed to poor trial design. This meant taking Actrapid at 30 minutes prior to a meal and it would clearly have been ludicrous to write on a clinical trial protocol that patients should inject Human Actrapid 29 minutes and 59 seconds prior to a meal to fall within the SPC. Furthermore the timings of the injections in these trials were approved by numerous independent ethics committees and notified to the Medicines Control Agency (MCA). The precedent referred to, Case AUTH/903/7/99, concerned advising patients to take their insulin up to 45 minutes prior to a meal. Without wishing to cover old ground, Novo Nordisk considered that there was a safety issue here in that the 45 minute delay seemed to run a risk of hypoglycaemia prior to the ensuing meal.

PANEL RULING

The Panel noted that in Case AUTH/903/7/99 a leavepiece for Lilly's product Humalog Mix25 had contained a table which had compared injection timing and insulin activity of Humalog Mix25 and human 30/70 insulins. Novo Nordisk noted that, with regard to the timing of human 30/70 insulin injections, the table stated '30-45 minutes before a meal' which was contrary to the advice given in its SPC for Human Mixtard. The table of data referred to human 30/70 insulins generally and so the statement that it should be injected 30-45 minutes before a meal would be taken to apply to all presentations of the product. The SPC for Novo Nordisk's human 30/70 insulin however clearly stated that it should be followed by a meal within 30 minutes of administration. The advice given in the table was therefore misleading with regard to the Novo Nordisk product and a breach of Clause 7.2 was ruled.

In the case now before it the Panel noted that the foreword was written by an independent expert and that it was his opinion on the progress being made in the treatment of diabetes by the introduction of new insulin. The product monograph was, however, promotional material and Novo Nordisk was responsible for its contents and the claims therein including the foreword. The statement that soluble human insulin worked best when given 30 minutes or more before meals would be taken to apply to all presentations of the product including Novo Nordisk's Actrapid which, according to its SPC, should be followed by a meal within 30 minutes of administration. The foreword was thus misleading with regard to Novo Nordisk's product and a breach of Clause 7.2 was ruled.

2 Suppressed zeros

COMPLAINT

Lilly noted that graphs illustrating the improvements in HbA_{1C} were present on pages 29 (figure 18) and 32 (figure 21). Once more a suppressed zero was used to exaggerate the data (Clause 7.6).

Suppressed zeros also featured in figures 12, 15, 16, 22 and 23.

RESPONSE

Novo Nordisk stated that with regard to the graphs on pages 29 and 32, it again, for the reasons outlined in point A1 above, strongly refuted the allegation that it had attempted to suppress the zeros on the y axes.

In each of figures 12, 16, 21, 22 and 23 there were two parallel diagonal lines clearly indicating a break in the y axes which should not in any way mislead a reader. Consultant physicians/diabetologists, pharmacologists and pharmacists would know that, for many of the graphs, a value of zero was meaningless (eg blood glucose or HbA_{1C} values) since a value of 0 did not occur in clinical practice. There were parallel break lines on the y axis in figure 15 which was comparing the upper values of blood glucose (post-prandial glucose peaks) and not the lower values but Novo Nordisk did not feel that this was in any way misleading to a professional readership. The scales on all of the y axes were clear and stood out against the dark blue background and Novo Nordisk did not believe that these graphs were in breach of Clause 7.6 of the Code.

PANEL RULING

The Panel noted that the graph on page 32 was identical to that considered in point A1 above. The

graph on page 29 was very similar albeit that it charted metabolic control with NovoRapid and human soluble insulin over a period of only 6 months and not 12. The Panel referred to its comments in point A1 and considered that its ruling of a breach of Clause 7.6 also applied here.

Figures 12, 15 and 16 were graphs which dealt with serum glucose levels (mmol/l). The y axis in two of the figures, 12 and 16, started at 4 whilst in figure 15 it started at 6. The Panel considered that the suppressed zeros gave a misleading impressing with regard to the impact of treatment on glycaemic control and ruled a breach of Clause 7.6.

Figures 22 and 23 were bar charts both with suppressed zeros. Figure 22 was almost identical to the bar charts considered in point A1 above. The Panel referred to its comments in point A1 and considered that its ruling of a breach of Clause 7.6 also applied here.

3 Prescribing information

COMPLAINT

Lilly noted that Insulatard, a Novo Nordisk product, was mentioned on page 25. This was clearly promotional advocating its used with NovoRapid. No prescribing information had been supplied (Clause 4.1).

RESPONSE

Novo Nordisk stated that Insulatard was mentioned on page 25 but no claim was made for it and therefore prescribing information was not supplied, Clause 18.3 of the Code referred.

PANEL RULING

The Panel referred to its comments in point A2. The product monograph promoted the combined use of NovoRapid and Human Insulatard. A breach of Clause 4.1 was ruled.

4 Post-prandial control

COMPLAINT

Lilly stated that the claim for better post-prandial control in Type 2 diabetes was overstated in the summaries on pages 1, 13 and 23. Whilst Lilly accepted that many patients were non-compliant, there was no data showing a benefit for NovoRapid if patients followed accepted clinical recommendations to wait approximately 30 minutes before eating following injection (Clause 7.2).

RESPONSE

Novo Nordisk did not consider that the claim for better post-prandial control in Type 2 diabetes was overstated. Its study (Rosenfalck *et al* (1999)) showed NovoRapid had significantly improved post-prandial glucose control compared to Actrapid in Type 2 patients when Actrapid was administered immediately before the meal and a tendency to improved control when Actrapid was given 30 minutes before a meal. Studies had indicated that 70% of patients took soluble human insulin close to or immediately before a meal. This statement reflected the reality of being a patient with diabetes and therefore it was useful to demonstrate the effectiveness of NovoRapid in post-prandial control over human soluble insulin injected immediately prior to a meal.

PANEL RULING

The Panel noted that the study by Rosenfalck *et al* had shown that immediate pre-meal administration of NovoRapid in patients with Type 2 diabetes resulted in an improved post-prandial glucose control compared to Actrapid injected immediately before a meal ($p=0.01$), but similar control compared to Actrapid injected 30 minutes before the meal.

The Panel noted that on page 1 the product monograph stated that NovoRapid provided significantly better post-prandial glucose control than soluble human insulin in Type 1 and Type 2 diabetes. Page 23 stated that NovoRapid had clear benefits over soluble human insulin and provided improved control of post-prandial glucose levels in Type 1 and Type 2 diabetes. The Panel considered that these claims would be taken to mean that, with regard to Type 2 diabetes, NovoRapid always provided better post-prandial glucose control than soluble human insulin which was not the case. When human soluble insulin was administered 30 minutes before a meal the effect of the two insulins were similar. Although the majority of diabetic patients injected human soluble insulin close to or immediately before a meal, in which case NovoRapid provided the better control, the claims in question had not referred to the importance of the timing of such injections.

The claims were thus misleading and a breach of Clause 7.2 was ruled.

The Panel noted that the claim on page 13, 'NovoRapid is thus well suited to the control of post-prandial glucose excursions in people with Type 1 and Type 2 diabetes', was not a comparison with human soluble insulin. The data showed that NovoRapid did control post-prandial glucose levels in Type 2 diabetics and so no breach of Clause 7.2 of the Code was ruled.

5 Claim '…clear benefits over soluble insulin in terms of … hypoglycaemic events…'

COMPLAINT

Lilly stated that on page 23 in the summary of the section 'NovoRapid in the clinical management of diabetes', there was the claim for '…clear benefits over soluble insulin in terms of …hypoglycaemic events …'. There was no statistically significant data to support an overall reduction in hypoglycaemia, only major nocturnal hypoglycaemia. The statement exaggerated the data and needed to be qualified (Clause 7.2).

RESPONSE

Novo Nordisk stated that on page 23 the qualification of the reduction in hypoglycaemic events occurred in the same paragraph and, therefore, the company considered that it met Lilly's stipulation and in doing so did not make an over-claim.

PANEL RULING

The Panel noted that the summary on page 23 began 'Clinical trials with NovoRapid have shown that it has clear benefits over soluble human insulin in terms of … hypoglycaemic events …'. In the Panel's view this implied that NovoRapid was of clear benefit with regard to all types of hypoglycaemia which was not so. The first sentence of the summary was qualified by the sixth which stated that the risk of major nocturnal hypoglycaemia was significantly reduced by NovoRapid compared with human soluble insulin.

The Panel noted that it was an accepted principle under the Code that misleading claims could not be qualified elsewhere in a piece. The first sentence of the summary gave a misleading impression as to the effect of NovoRapid on hypoglycaemia and a breach of Clause 7.2 was ruled.

6 Claim '… NovoRapid is likely to result in a lower risk of hypoglycaemia between meals'

COMPLAINT

Lilly stated that the statement on page 42 that '…NovoRapid is likely to result in a lower risk of hypoglycaemia between meals …' was highly speculative and unsubstantiated. There was no clinical data to support this claim, which again could not be predicted from pharmacokinetic and pharmacodynamic data (Clause 7.3).

RESPONSE

Novo Nordisk stated that the statement that '…NovoRapid is likely to result in a lower risk of hypoglycaemia between meals' was not highly speculative and was based on Novo Nordisk's knowledge of the pharmacokinetic profile and pharmacodynamic action of NovoRapid. By using the word 'likely' Novo Nordisk was not making a statement of absolute fact but rather conveying the strong belief of the experts who had advised it on the basis of Novo Nordisk's clinical studies. Novo Nordisk knew that the maximum duration of action of NovoRapid was 5 hours with the peak effect occurring between 1-3 hours. This was a more physiological action profile than injected soluble human insulin which had a duration of action of up to 8 hours and could cause hypoglycaemia in the late post-prandial period (pre-meal) and also during the night.

PANEL RULING

The Panel noted that the statement regarding the lower risk of hypoglycaemia between meals was based on the known pharmacokinetic profile and pharmacodynamic action of NovoRapid. It was not based on clinical data. The Panel referred to its comments in B above. A breach of Clause 7.2 was ruled.

7 Alleged promotion outside licence

COMPLAINT

Lilly noted that on page 40, the section on use in pregnancy appeared to be promoting use of NovoRapid outside the licence. In particular, the sentence 'As with any insulin therapy, adjustments to dose and regimen may need to be made …' was promoting the use of NovoRapid (Clause 7.2).

RESPONSE

Novo Nordisk considered that the section on pregnancy was in line with the SPC for NovoRapid and did not attempt to promote its use in pregnancy. No insulin had a licence for use in pregnancy but oral agents were generally contraindicated in pregnancy because of the risk of teratogenicity. The wording regarding dosage adjustments simply reflected the second sentence in the third paragraph in the SPC for NovoRapid.

PANEL RULING

The Panel noted that the NovoRapid SPC stated that it was for the treatment of patients with diabetes mellitus. Section 4.6 of the SPC 'Pregnancy and lactation' stated that there was limited use of the product in pregnancy. Animal reproduction studies had not revealed any differences between NovoRapid and human insulin regarding embryotoxicity or teratogenicity. It was also stated that intensified monitoring of pregnant women with diabetes was recommended throughout pregnancy; insulin requirements usually fell in the first trimester and increased subsequently during the second and third trimesters.

The statement in the product monograph expanded on the information given in the SPC to state that a small number of pregnancies occurred in women using NovoRapid during the clinical study programme but proceeded without giving cause for concern. No studies had specifically studied the use of NovoRapid in pregnant women.

The Panel noted that the NovoRapid SPC did not contain any prohibition or restriction on the use of the product during pregnancy. The product monograph had expanded on the information given in the SPC but was not inconsistent with it. The Panel did not consider that the product monograph promoted NovoRapid outside the terms of its licence and ruled no breach of Clause 3.2.

The Panel noted that Lilly had alleged a breach of Clause 7.2 but considered that promotion of a medicine outside the terms of its licence was more properly considered under Clause 3.2 of the Code.

Complaint received **20 October 1999**

Case completed **17 January 2000**

CONSULTANT PSYCHIATRIST v LOREX SYNTHÉLABO

Solian 'Dear Doctor' letter

A consultant psychiatrist complained about a Solian (amisulpride) 'Dear Doctor' letter which had been sent to him by Lorex Synthélabo. An accompanying leaflet depicted a young woman with schizophrenia and reported her landlady's reaction to her not paying the rent or keeping her home clean and posed the question 'What do you need to bring her back?' The letter headed 'The challenge: bringing her back' began 'When you look at the enclosed leaflet, I know your sympathy will be with this confused, disturbed, disorganised lady with acute-phase schizophrenia who is seen to be coping so badly with the basic routine of living. Yet her landlady's angry, abusive reactions are understandable, if hurtful and unhelpful. This young patient needs to be able to take her place in the community, without living in a pigsty or alienating everyone else in the world around her'. The complainant alleged that the letter was offensive and stigmatising in its remarks about people with severe mental illness. In particular, he considered that it was improper, merely in order to prompt him to prescribe Solian, to tell him that a 'young patient needs to be able to take her place in the community, without living in a pigsty'.

The Panel noted that Solian was indicated for the treatment of acute and chronic schizophrenic disorders in which positive and/or negative symptoms were prominent. The 'Dear Doctor' letter discussed the efficacy of Solian under the headings a fast response, a reliable response and an effective response, and concluded that Solian 'can help a patient like this to find – and keep – her footing in today's often unforgiving and hard-nosed environment.' The Panel considered that this was difficult area. The letter attempted to provide a realistic portrayal of society's reaction to a patient with acute-phase schizophrenia and the description was relevant to the therapeutic area. The Panel considered that matters of taste were subjective and attitudes would differ. The Panel accepted that the letter would offend some recipients. It did not, however, consider that the majority would find it objectionable and ruled no breach of the Code.

A senior lecturer in psychiatry and honorary consultant psychiatrist complained about a Solian (amisulpride) 'Dear Doctor' letter (ref SOL.100/L) sent to him by Lorex Synthélabo UK & Ireland Ltd. The letter had been sent to general and old age psychiatrists of the following grades: consultant, associate specialist, staff, specialist registrar and registrar.

A leaflet (ref SOL.100/M), which accompanied the 'Dear Doctor' letter, depicted a young woman with schizophrenia and reported her landlady's reaction to her not paying the rent or keeping her home clean and posed the question 'What do you need to bring her back?'. The letter headed 'The challenge: bringing her back' began 'When you look at the enclosed leaflet, I know your sympathy will be with this confused, disturbed, disorganised lady with acute-phase schizophrenia who is seen to be coping so badly with the basic routine of living. Yet her landlady's angry, abusive reactions are understandable, if hurtful and unhelpful. This young patient needs to be able to take her place in the community, without living in a pigsty or alienating everyone else in the world around her'.

The letter of complaint was sent to Lorex Synthélabo and copied to the Authority.

COMPLAINT

The complainant alleged that the 'Dear Doctor' letter was offensive and stigmatising in its remarks about people with severe mental illness. In particular, he considered that it was improper, merely in order to prompt him to prescribe Solian, to tell him that a 'young patient needs to be able to take her place in the community, without living in a pigsty'.

The complainant stated that derogatory caricatures of people with mental illness were damaging additions to the severe stigma which was already prevalent. He noted that the Broadcasting Standards Commission had recently judged against the Channel 4 programme 'Psychos', finding the advertising of the series offensive to those suffering from mental health problems. The promotion of medicines to treat mental illness required proper standards too. Writing to doctors about patients living in a pigsty was wrong and could not fall within the terms of Clause 9.1 of the Code which described a higher standard for suitability and taste in marketing medicines than might be acceptable more generally.

RESPONSE

Lorex Synthélabo expressed regret that the complainant had been offended by the 'Dear Doctor' letter. However, the letter was accompanied by a leaflet and was not intended to be taken out of context.

Lorex Synthélabo stated that the letter clearly referred to the enclosed leaflet and that the letter was clearly not seeking to stigmatise people suffering from schizophrenia or suggest that all such sufferers lived in a pigsty. The sentence quoted, from the end of the first paragraph, referred to the enclosed leaflet and did not contravene acceptable standards.

The leaflet which accompanied the letter described a situation in which a young person suffering from schizophrenia was subjected to abuse. This was a description of a situation that could and did occur. Lorex Synthélabo stated that the letter should be read in its entirety and should not be dissected. The letter did not seek to degrade or stigmatise the person

suffering from schizophrenia and the company did not consider that it did. The tone of the letter was of sympathy with the young lady and it was clearly stated that the doctor would sympathise too.

Lorex Synthélabo did not consider that the letter was in breach of Clause 9.1 of the Code.

PANEL RULING

The Panel noted that Clause 9.1 required that all material and activities must recognise the special nature of medicines and the professional standing of the audience to which they were directed and must not be likely to cause offence.

The Panel noted that Solian was indicated for the treatment of acute and chronic schizophrenic disorders in which positive and/or negative symptoms were prominent. The 'Dear Doctor' letter discussed the efficacy of Solian under the headings a fast response, a reliable response and an effective response and concluded that Solian 'can help a patient like this to find – and keep – her footing in today's often unforgiving and hard-nosed environment.'

The Panel considered that this was a difficult area. The Panel noted that the letter attempted to provide a realistic portrayal of society's reaction to a patient with acute-phase schizophrenia. The description was relevant to the therapeutic area. The mailing was sent to a professional audience.

The Panel considered that matters of taste were subjective and attitudes would differ. Whilst the Panel accepted that the letter would offend some recipients, it did not, however, consider that the majority would find it objectionable and ruled no breach of Clause 9.1 of the Code.

Complaint received **20 October 1999**

Case completed **26 November 1999**

CASE AUTH/948/10/99

GENERAL PRACTITIONER v BAYER

Conduct of representative

A general practitioner complained that in meetings and a telephone call with nurses at the practice, a representative from Bayer had offered a finger prick cholesterol testing device in return for a commitment to prescribe Lipobay.

The Panel noted that Bayer had acknowledged that its representative had overstepped the mark. The representative had offered an inducement to prescribe Lipobay and this was totally unacceptable and a breach of the Code was ruled. A further breach was ruled because the representative had failed to maintain a high standard of ethical conduct and comply with the Code. The Panel considered that the representative's conduct brought discredit upon and reduced confidence in the pharmaceutical industry and a breach of Clause 2 was ruled.

A general practitioner complained about the conduct of a representative from Bayer plc, Pharmaceutical Division. The matter involved the provision of a cholesterol testing device to certain practices as part of a Bayer initiative called the Change of Heart Programme. Bayer stated that the aim of the programme was to help practices meet their targets for the treatment of coronary heart disease whilst enabling them to gain experience in the use of Lipobay (cerivastatin) and Adalat LA (nifedipine).

The complainant had written a letter of complaint to Bayer and copied it with a covering letter to the Authority.

COMPLAINT

The complainant outlined the conduct of the representative, who was a new employee in his first job, as follows:

First meeting with two of the practice nurses:
The representative asked the practice nurses if they would like a finger prick cholesterol device and suggested a target group of patients (eg those with ischaemic heart disease). Bayer would provide stamps etc to send letters and would help in the clinic. The representative asked for a commitment to prescribe Lipobay as each testing cassette cost over £8. The nurses agreed that they did not want to have clinics but would be happy to have the machine for opportunistic screening for a couple of weeks and would discuss it with the GPs first. The representative was told there would be no commitment to prescribe Bayer's medicines. The representative made arrangements to return in two weeks.

Second meeting with same two practice nurses two weeks later:
The representative told the nurses that he had been made redundant and was leaving the company but was still committed to an arrangement with the practice. He said sales figures were too low in this area and Bayer wanted to put in a more experienced representative. He was told that the practice definitely would not be running cholesterol clinics or promise to prescribe Lipobay but that the practice was still interested in opportunistic screening. Again the nurses were told about cost of cassettes and one nurse told the representative that that was not her concern.

The representative said that he would discuss it with his manager.

Telephone call to senior practice nurse one week later:
The representative said that the manager was very keen for the practice to do opportunistic screening and asked how many people would be recruited and how many of those could be prescribed Lipobay? The representative again told the nurse how expensive each cassette was. The nurse told the representative very clearly that the practice would not have the machine on that basis. The nurse used the 24 hour BP machine loan as illustration of how other companies work and told the representative very politely to go away.

The complainant stated that the practice was very unhappy about the implications that in order to have a machine the doctors should prescribe Lipobay. The practice alleged that this was contrary to the Code.

RESPONSE

Bayer acknowledged that it would appear that its representative had overstepped the mark. The company certainly did not condone the linking of assistance in setting up cardiovascular risk clinics to commitment to prescribing any of its products, and it considered that the representatives' briefing material supported this position. In particular the company drew attention to statements which read 'We cannot link the offer of help to run a CV [cardiovascular] risk clinic directly to a 'demand' for prescriptions of our products – this is a contravention of the Code of Practice', 'We cannot insist that Lipobay is used …' and '…we cannot directly link the offer of the Change of Heart Programme to a 'demand' for Lipobay prescriptions'. A copy of the representative's briefing material was provided. All representatives were fully briefed on the Change of Heart Programme and how it should be implemented. The company submitted that the programme itself complied with the Code.

Bayer stated that the representative concerned had been in the industry for only six months and had been on a fixed-term contract with Bayer, which the company had not renewed; he had now left Bayer's employment. The representative had not sat the ABPI Representatives Examination; however, he received a comprehensive briefing on the Code as part of his initial training.

Bayer could only assume that the representative's enthusiasm got the better of him and hence the apparent breach of the Code.

The company apologised unreservedly for the breach of the Code and assured the Authority that this was an isolated case.

PANEL RULING

The Panel noted that the complainant alleged that, at a meeting with two practice nurses, the Bayer representative had offered a cholesterol finger prick device but in return had asked for a commitment to prescribe Lipobay as each testing cassette cost over £8. The representative had also asked during a telephone conversation about the number of people who would be recruited for opportunistic screening and how many of those could be prescribed Lipobay. Bayer acknowledged that it appeared that the representative had overstepped the mark. The company did not condone the linking of assistance in establishing CV risk clinics to commitment to prescribing any of the company's products. Bayer submitted that the documentation supported its position.

The Panel considered that the provision of the cholesterol testing device had clearly been linked to a commitment to prescribe Lipobay. The representative had offered an inducement to prescribe Lipobay and this was totally unacceptable. A breach of Clause 18.1 of the Code was ruled. Further the representative had failed to maintain a high standard of ethical conduct and comply with the Code. The Panel therefore ruled a breach of Clause 15.2 of the Code.

The Panel also considered that the representative's conduct brought discredit upon and reduced confidence in the pharmaceutical industry and a breach of Clause 2 was ruled.

Complaint received	**25 October 1999**
Case completed	**24 November 1999**

CASE AUTH/949/10/99

SOCIAL AUDIT v PHARMACIA & UPJOHN

Detrusitol journal advertisement

Social Audit submitted a complaint about a journal advertisement for Detrusitol issued by Pharmacia & Upjohn.

The complainant pointed out that the advertisement included claims such as 'Freed by Detrusitol', 'help free your patients from the restrictions of unstable bladder' and 'Detrusitol effectively and selectively relieves frequency, urgency and/or urge incontinence'. The complainant alleged that such claims appeared to apply only to a small percentage of treated patients. Reference was made to a table of data in the summary of product characteristics (SPC). The complainant alleged that the advertisement was not strictly accurate, nor balanced nor fair to either doctors or patients, not objective and far from unambiguous.

The Panel noted that Detrusitol was licensed for the treatment of unstable bladder with symptoms of urgency, frequency and urge incontinence. The Panel examined the data and considered that whilst Detrusitol had been shown to help improve quality of life patients continued to report some degree of bladder problems. The most prominent claim 'Freed by Detrusitol' created the impression that treatment would result in patients having no symptoms of urgency, frequency or urge incontinence, which was not the case. The claim 'Detrusitol effectively and selectively relieves frequency, urgency and/or urge incontinence' would be read similarly. The Panel considered that 'Freed by Detrusitol' overstated the totality of the efficacy data and was not balanced. A breach of the Code was ruled.

Social Audit submitted a complaint about an advertisement (ref P4483R/5/99) for Detrusitol (tolterodine) produced by Pharmacia & Upjohn Limited which appeared in the BMJ 23 October 1999. The advertisement, which was headed 'Freed by Detrusitol', featured a photograph of an older women sitting by a swimming pool. Beneath the photograph was the claim 'Detrusitol effectively and selectively relieves frequency, urgency and/or urge incontinence. With simple b.d. dosing.' The strapline 'Help free your patients from the restrictions of unstable bladder' appeared beneath the product logo.

COMPLAINT

The complainant queried whether the claims in the advertisement complied with Clause 7.2 of the Code. The reason for doubting it was that the advertisement failed to reflect the important evidence relating to lack of efficacy and/or the modest effect of the medicine that appeared in a table in the summary of product characteristics (SPC). This indicated that fewer than two patients in ten experienced 'no or minimal bladder problems after treatment' – very few more than the numbers who recovered without the medicine (ie on placebo).

The advertisement included prominent claims such as, 'Freed by Detrusitol', 'Help free your patients from the restrictions of unstable bladder', and 'Detrusitol effectively and selectively relieves frequency, urgency and/or urge incontinence'. Such claims would seem to apply to only a small percentage of the patients treated with this medicine; the complainant's contention was that doctors would need to know this, and that the advertisement was not strictly accurate, nor balanced, nor fair to either doctors or patients, not objective, and far from unambiguous.

RESPONSE

Pharmacia & Upjohn addressed each claim referred to by the complainant in turn.

1 'Detrusitol effectively and selectively relieves frequency, urgency and/or urge incontinence'

Detrusitol had been given a product licence for 'the treatment of unstable bladder with symptoms of urgency, frequency and urge incontinence', the efficacy data for Detrusitol having been reviewed by the Medicines Control Agency (MCA) in the European Mutual Recognition procedure in 1997. Owing to the fact that the inclusion criteria for the Phase III clinical trials for Detrusitol were almost identical in each study, the pooled results for the four 12 week studies were accepted by the MCA as valid data to assess the efficacy of the medicine. This data was presented in the Detrusitol SPC, and was also published (Appell (1997)). In this publication, it was reported:

a) For the primary efficacy variable, the number of micturitions/24 hours (indicating urinary frequency), a significant decrease from baseline, compared with placebo, was seen for the 1mg tolterodine ($p<0.001$), 2mg tolterodine ($p<0.001$). Each active treatment group reduced mean daily micturition frequency by approximately 20% from the baseline mean.

b) For the number of incontinence episodes/24 hours, pooled results showed a significant decrease from baseline for both tolterodine doses compared to placebo ($p<0.05$), with a 47% reduction in incontinence episodes for the patients treated with Detrusitol 2mg bd.

c) For the mean volume voided per micturition, which gave a clinical representation of bladder capacity, pooled results showed a significant increase from baseline for both tolterodine doses compared to placebo ($p<0.001$), with a 22% increase in mean volume voided/micturition for the patients treated with Detrusitol 2mg bd.

Similar results were found in individual studies, the published results of two of these studies having been used as references in the advertisement, Malone-Lee *et al* (1997) and Abrams *et al* (1998). In addition, the data from long-term open label studies with Detrusitol showed that the number of micturitions/24 hours, the number of incontinence episodes/24 hours, and the mean volume voided/micturition all improved

markedly from baseline to six months and that this effect was maintained during the rest of the study and remained at the end of the treatment period of 12 months (Messelink (1999)).

Urgency was not measured during the Phase III clinical trials as this variable was considered to be subjective, in addition to the fact that a large number of patients with unstable bladder void frequently to avoid the sensation of urgency occurring. Therefore frequency was considered to be the more favourable efficacy variable. However, the MCA accepted that urgency was part of the symptom complex of unstable bladder, therefore Detrusitol was licensed for the treatment of frequency and urgency.

Thus Pharmacia & Upjohn submitted that it could be seen that Detrusitol did effectively relieve frequency, urgency and/or urge incontinence.

The promotion for Detrusitol as being selective for the bladder in the treatment of detrusor instability was consistent with the SPC which stated under section 5.1, Pharmacodynamic Properties, that 'tolterodine is a specific cholinergic receptor antagonist with a selectivity for the urinary bladder rather than the salivary glands in vivo'. Pharmacia & Upjohn referred to the relevant pages in the Pharmacological and Toxicological Expert Report for tolterodine.

Cholinergic, muscarinic receptors were thought to be the prime mediators of detrusor muscle contractions, and therefore blocking these receptors with anticholinergic, antimuscarinic medicines decreased the activity of the overactive detrusor muscle – thus improving the symptoms of unstable bladder, ie frequency, urgency and/or urge incontinence. In pre-clinical trials the binding of tolterodine and DD01 (the only metabolite with significant activity) was tested at more than 50 receptors and binding sites; the results of these tests indicated that Detrusitol and DD01 were pure and specific muscarinic receptor antagonists, with negligible effects at other potential cellular targets. The risks of side effects from the medicine affecting other receptors in other organs were thus reduced.

Five sub-types of muscarinic receptor had been identified molecularly (m_1-m_5), four of which had been identified pharmacologically (M_1-M_4). The bladder contained a mixed population of M_2 and M_3 receptors, constituting approximately 80% and 20% respectively of the total muscarinic receptor population in the bladder. Despite the M_3 receptors being in the minority, it had always previously been considered that the M_3 receptors were the prime mediators of detrusor muscle contractions. Thus many medicines that had previously been licensed for treatment of the unstable detrusor muscle, including oxybutynin, and others in development for unstable bladder, for example darifenacin, had been M_3 selective. The problem was that the salivary glands were also rich in M_3 receptors, thus whilst M_3 selective drugs inhibited the unwanted overactive detrusor muscle contractions, they also inhibited the salivary glands – causing a dry mouth. These M_3 selective medicines were therefore not organ selective for the bladder, as they also affected the salivary glands to a high degree.

In Pharmacia & Upjohn's pre-clinical studies, it was discovered that tolterodine was not selective for any of the muscarinic receptor sub-types. However, whereas tolterodine was found to be equipotent to oxybutynin with respect to the inhibition of detrusor muscle contractions, oxybutynin bound to the muscarinic receptors in the salivary glands with 8-times higher affinity than tolterodine (Nilvebrant *et al* (1997a) and Nilvebrant *et al* (1997b)), presumably due to the higher impact of oxybutynin on the M_3 receptors in the salivary glands. Pharmacia & Upjohn referred to two graphs taken from Nilvebrant *et al* (1997a) which showed the impact of tolterodine and oxybutynin on both the inhibition of detrusor muscle contractions and salivation in the anaesthetised cat.

Whereas with oxybutynin it was not possible to obtain inhibition of the detrusor muscle contractions without a significant inhibition of the salivary glands, with tolterodine, throughout most of the pre-clinical dose range, the inhibition of the detrusor muscle contractions could be obtained with a much reduced inhibition of the salivary glands. The organ selectivity of tolterodine for the bladder *in vivo* could not be attributed to a single muscarinic receptor sub-type. However the combined *in vitro* and *in vivo* data on tolterodine and oxybutynin might indicate either that muscarinic M_3 receptors in salivary glands were more sensitive to blockade than those in bladder smooth muscle, or that the role of the M_2 receptors in the bladder, which tolterodine was also blocking, might have previously been underestimated, and that they were also contributing to the detrusor muscle contractions. Indeed, it had been proposed that the M_2 receptors had a function of reversing sympathetically mediated detrusor relaxation (Hegde *et al* (1997)) – ie blockade of these receptors caused relaxation of the overactive detrusor muscle. This would account for the effect of tolterodine on the detrusor muscle being equivalent to that of oxybutynin, despite lack of muscarinic receptor selectivity. However the decreased effect on the salivary glands accounted for the organ selectivity of tolterodine.

The pharmacological basis for the organ selectivity of Detrusitol had therefore been clearly demonstrated, resulting in a clinical activity of the inhibition of overactive detrusor muscle contractions with an equal efficacy to oxybutynin, the gold standard treatment for unstable bladder, but with a much reduced clinical effect on the salivary glands. This was demonstrated in a Phase I tolterodine study, looking at urodynamic variables in addition to subjective outcome measures, the results of which suggested that a selective effect on the bladder, as demonstrated in an animal model, could also be obtained in humans, (Stahl *et al* (1995)). In addition, the Phase II data was pooled, and the results illustrated that although treatment with tolterodine caused dose-related improvements in micturition diary and urodynamic variables, the main adverse effects of tolterodine were non-serious, mild or moderate antimuscarinic effects, with no patients withdrawing from treatment as a result of antimuscarinic adverse events other than urinary retention (Larsson *et al* (1999)). Likewise the tolterodine Phase III data revealed that tolterodine had an equal efficacy to oxybutynin on the symptoms of unstable bladder, with a much improved tolerability profile (Appell (1997)).

Thus Detrusitol had been clearly shown in both pre-clinical and clinical studies to have organ selectivity for the bladder. This had been accepted by the regulatory bodies of the EU member states when approving the wording in the SPC, which confirmed the selectivity of Detrusitol.

2 Claims: ' Freed By Detrusitol' and 'Help Free Your Patients from the Restrictions of Unstable Bladder'

Pharmacia & Upjohn stated that unstable bladder was known to severely restrict the lives of patients, not just because of urge incontinence which could often be managed with the use of containment products, but more importantly because of the frequency and urgency of micturitions from which patients suffered. Frequency could be defined as passing urine ≥8 times per 24 hours, thus typically a patient might pass urine 12 times during the day and get up three times at night to pass urine. Owing to the urgency associated with these frequent micturitions, patients were often afraid to go out, gave up work, and could become socially isolated. The quality of life of patients suffering with unstable (overactive) bladder had been studied using various quality of life instruments, and a recent publication showed that Short Form 36 scores for patients with overactive bladder were significantly lower than those of the normal population ($p<0.001$). This paper also showed that when a disease specific quality of life instrument was utilised, in this case the Kings Health Questionnaire, the quality of life of patients suffering with overactive bladder was significantly improved with treatment with tolterodine. This was more clearly seen in the Data on File, (Study 031(UK)) for one of the studies on which this paper was written – which showed that treatment with tolterodine resulted in a significant improvement in the following quality of life domains; emotions, incontinence impact, physical limitations, role limitations, severity measures, sleep/energy and social limitations. If a patient had a frequency of 15 micturitions per 24 hours, Detrusitol – as illustrated earlier – could be expected to decrease the frequency by 20%. This would lead to a longer time between each micturition, with less urgency, enabling patients to perform tasks they had previously been unable to do – freeing up their lives.

A classic patient history and testimonial was published in the 'You' magazine on 31 October 1999. A patient reported her history of treatment with both oxybutynin and Detrusitol, and although she still suffered from incontinence she reported 'I can now last up to four hours without needing to go to the toilet. I've got my life back again'.

Clearly freedom from the restrictions of unstable bladder involved more than simply making incontinent patients dry, it involved decreasing frequency and urgency such that patients could restart their normal activities and improve their quality of life. This had undoubtedly been shown in studies with Detrusitol, which did improve patients' quality of life and their ability to perform normal activities, freeing them from the restrictions of unstable bladder.

Pharmacia & Upjohn, therefore, believed the claims for Detrusitol in the above mentioned advertisement were accurate, balanced, objective and it certainly believed the claims were not ambiguous and not to be in breach of the Code.

PANEL RULING

The Panel noted that Detrusitol was indicated for the treatment of unstable bladder with symptoms of urgency, frequency or urge incontinence.

Data presented in the Detrusitol SPC from 12 week studies showed a statistically significant decrease from baseline, compared to placebo, in the number of micturitions per 24 hours ($p\leq0.01$), the number of incontinence episodes/24 hours ($p\leq0.05$) and a statistically significant increase from baseline in the mean volume voided per micturition. There was no statistically significant difference as against placebo in the percentage of patients with no or minimal bladder problems after treatment at 12 weeks. The 4 week studies showed a statistically significant difference between placebo and Detrusitol in relation to the number of patients with none or minimal bladder problems after treatment ($p\leq0.01$). Malone-Lee *et al* (1997) demonstrated a significant effect on incontinence and increase in volume voided at 2mg. Abrams *et al* (1998) showed a significant effect on the frequency of micturition and volume voided but not on the number of incontinence episodes. The Panel noted that Kobelt *et al* (1999) was a review, which discussed quality of life aspects of the overactive bladder and the effect of treatment with tolterodine and concluded that tolterodine had the potential to increase compliance with treatment and thus patients' overall well-being. The Panel also noted the Kings Health Questionnaire. The Panel considered that whilst Detrusitol had been shown to help improve quality of life patients continued to report some degree of bladder problems.

The Panel considered that the heading and most prominent claim, 'Freed by Detrusitol' was a strong statement. 'Freed' was an absolute term and the claim created the impression that treatment with Detrusitol would result in patients having no symptoms of urgency, frequency or urge incontinence which was not the case. The heading set the tone for the advertisement and dictated how other claims within it would be read. In the Panel's view the word 'relieves' in the claim 'Detrusitol effectively and selectively relieves frequency, urgency and/or urge incontinence' would be read in the same way as 'Freed' in the heading. The Panel noted that the strapline 'Help free your patients from the restrictions of unstable bladder' was a more qualified claim but it was not sufficient to negate the overall impression of the advertisement.

In the Panel's view the complainant was concerned that the efficacy of Detrusitol had been overstated and was not questioning its pharmacological selectivity. The Panel considered that 'Freed by Detrusitol' overstated the totality of the efficacy data and was not balanced. A breach of Clause 7.2 was ruled.

Complaint received **28 October 1999**

Case completed **4 January 2000**

CASE AUTH/950/10/99

PASTEUR MÉRIEUX MSD v SMITHKLINE BEECHAM

Free postage paid envelopes

Pasteur Mérieux MSD complained about the provision by SmithKline Beecham to its customers of second class postage paid envelopes. SmithKline Beecham's justification for this was that the envelopes were to be used for recalling patients for booster doses of hepatitis A vaccine. Pasteur Mérieux alleged that there was no clear link between the postage paid envelopes and their intended use and that they could be seen as a financial inducement.

The Panel noted that the envelope could be used by the practice for any mailing. Pasteur Mérieux had made the point that there was no clear link between the postage paid envelope and its intended use. A pack containing template reminder letters, travel vaccination questionnaires and practice health check lists, together with the postage paid envelopes, was provided by representatives following a request from the practice. There were no instructions about the use of the pack. The Panel did not consider that it was acceptable to, in effect, supply postage stamps to practices. The Panel ruled that the supply of the envelopes was unacceptable and a breach of the Code was ruled.

COMPLAINT

Pasteur Mérieux MSD Ltd complained about the provision by SmithKline Beecham Pharmaceuticals of second class postage paid envelopes to its customers (a copy of an envelope was provided). SmithKline Beecham had stated that its justification for this was that the envelopes were to be used for recalling patients for booster doses of hepatitis A vaccine. However Pasteur Mérieux alleged that there was no clear link between the postage paid envelopes and their intended use and was concerned that this practice, however well intentioned, could be seen as a financial inducement and was thus in breach of Clause 18.1 of the Code.

Pasteur Mérieux referred to the precedent set by Case COP/1054/10/91 in which a breach of Clause 19.1 [Clause 18.1 of the current Code] was ruled for supplying a free second class postage stamp with every dose of flu vaccine ordered. Whilst Pasteur Mérieux recognised the important role of patient recalls to the success of many vaccination schedules it was essential that any recall tool was unambiguously linked to that purpose alone.

RESPONSE

SmithKline Beecham stated that the second class postage paid envelopes at issue were supplied to general practices specifically as part of a booster vaccination campaign in keeping with an initiative aimed at enhancing patient care. For hepatitis A, uptake of booster vaccinations following a primary immunisation was poor and it had been recognised for some time that booster rates needed to be increased from their current low levels. Many GP surgeries had asked the company to provide assistance in ensuring adequate booster coverage.

For the hepatitis A booster vaccination SmithKline Beecham provided a series of items, this included a template for a booster vaccination reminder letter to patients, reply paid envelopes for return of a travel vaccination questionnaire, the questionnaire itself which detailed potential travel vaccination requirements in the next 12 months and a practice health check list which provided information on common diseases of travel. Practices were provided with sufficient materials for hepatitis A booster for approximately 20 patients at any one time, equivalent to a total cost to the company of less than £5, ie 20 envelopes at 22p each.

SmithKline Beecham's vaccine representatives visited many GP practices, only a proportion of which used its hepatitis A vaccine. All the services were available to all customers regardless of use of SmithKline Beecham's products.

Packs of template reminder letters, travel vaccination questionnaires and practice health check lists together with reply paid envelopes were provided by SmithKline Beecham representatives following a request from the practice. These could instead be mailed to the practice if requested.

The practice then mailed out the materials to the patients in the reply paid envelopes. Patients were then requested to return the questionnaires personally and make an appointment for a booster.

Briefing of representatives was done verbally by the medical director. It was considered unnecessary to provide specific written materials, as this matter did not relate to either the technical aspects of a specific medicine or to how a specific product was promoted.

SmithKline Beecham therefore believed that not only did this initiative comply with Clause 18.1 in providing medical and educational goods and services which would enhance patient care but also complied with Clause 18.2 if these envelopes were considered to be a gift in that they cost SmithKline Beecham less than £5.

PANEL RULING

The Panel noted that in Case COP/1054/10/91 a ruling equivalent to a breach of Clause 18.1 of the current Code was made in relation to the supply of a second class postage stamp with every dose of a flu vaccine ordered. The case now before it was different in that the supply of postage paid envelopes was not linked to the purchase of medicines.

The Panel examined the envelope. It was a plain white window envelope with second class postage paid. The Panel noted that the envelope could be used by the practice for any mailing. Pasteur

Mérieux had made the point that there was no clear link between the postage paid envelope and its intended use. The pack containing the template reminder letters, travel vaccination questionnaires and practice health check lists, together with the postage paid envelopes, was provided by representatives following a request from the practice. There were no instructions to healthcare professionals about the use of the pack.

The Panel considered that it might be acceptable for companies to provide materials etc to practices to recall patients. Such arrangements had to comply with the Code. The Panel did not consider that it was acceptable to, in effect, supply postage stamps to practices. The postage paid envelopes should have been more closely linked to their intended purpose. The Panel ruled that the supply of the postage paid envelopes was unacceptable. It noted that they cost less than £5. It was not acceptable to provide healthcare professionals with postage stamps. A breach of Clause 18.1 of the Code was ruled.

Complaint received **27 October 1999**

Case completed **18 January 2000**

CASE AUTH/951/11/99

PARKE DAVIS and PFIZER v MERCK SHARP & DOHME

Promotion of Zocor

Parke Davis and Pfizer complained about five promotional items for Zocor (simvastatin) issued by Merck Sharp & Dohme. Parke Davis and Pfizer co-marketed Lipitor (atorvastatin).

Parke Davis and Pfizer alleged that the claim 'Zocor enables up to 9 out of 10 CHD patients to reach the LDL cholesterol goal of <3mmol/l' was misleading, all embracing, not accurate and not capable of substantiation. The Panel noted that the claim had been complained about in two earlier cases, Cases AUTH/937/10/99 and AUTH/941/10/99, when it considered that the claim was misleading, exaggerated and not capable of substantiation. The Panel considered that its rulings of breaches of the Code would also apply here. In addition a breach was ruled as substantiation had not been provided to Parke Davis and Pfizer. Similar complaints were made about the use of similar, although slightly amended, claims in three journal advertisements, a price reduction letter and a mailing. The Panel ruled that all the items were in breach of the Code.

Parke Davis and Pfizer alleged that the claim 'Zocor is the only statin licensed to reduce cholesterol, triglycerides and to raise HDL-Cholesterol' which appeared in a price reduction letter was a factually incorrect exaggeration that was misleading. Lipitor (atorvastatin) was licensed to reduce cholesterol and triglycerides and, as of 24 September 1999, to raise HDL-cholesterol. Parke Davis and Pfizer alleged that the presribing information on the reverse of the letter was also incorrect. The letter highlighted new lower prices for Zocor whilst the prescribing information continued to refer to the old prices and was thus misleading. The letter also claimed that 'Zocor offers unique benefits to the NHS and patients through its unsurpassed survival data, efficacy across all lipid parameters, proven long-term tolerability and cost-effectiveness data.' This was alleged to imply a general superiority for simvastatin that was misleading. Dealing with each allegation in turn, the Panel noted that the claim in full was 'Zocor is also the only statin licensed to improve survival, lower cholesterol, triglycerides and raise HDL-Cholesterol'. The complainants had omitted the reference to improving survival. The Panel noted that the licence for Lipitor had been amended to include raising HDL-C. Lipitor was not licensed to improve survival. Zocor was the only statin licensed for the four features given in the claim. The Panel considered that the claim was not unacceptable and no breach of the Code was ruled. The Panel noted that the letter itself clearly gave the old prices for Zocor, the new price and the percentage price reduction. The prescribing information, included on the reverse of the letter, gave the old price. The Panel noted that guidance had been issued in the August 1999 Code of Practice Review with regard to price reductions as a result of the revised Pharmaceutical Price Regulation Scheme. The guidance stated that in the period 1 October to 31 December promotional material would not be considered to be in breach of the Code if it still carried the previous higher price. The Panel considered that the letter was covered by the guidance. Readers would be clear about the price changes. No breach of the Code was ruled. The Panel noted that it had already ruled on the use of 'unique' in an earlier case, Case AUTH/941/10/99. In the earlier case, the Panel considered that the word unique was used to imply a general superiority and this implied that Zocor had some special merit which could not be substantiated. The Panel considered that its rulings of breaches of the Code in the earlier case also applied here.

Parke Davis and Pfizer alleged that a claim in a mailer that 'The only statin licensed to reduce cholesterol, triglycerides and to raise HDL' was in breach of the Code as it was factually incorrect and misleading as atorvastatin was so licensed. A breach of the Code was alleged as the mailer consisted of more than four pages and there was no indication as to where the prescribing information could be found. The claim 'Zocor now gets more patients to goal at a lower price' was alleged to be all-embracing and also a hanging comparison. It suggested that simvastatin got more patients to their

goal than any other statin and that simvastatin got more patients to their goal more cheaply than with any other statin. Neither of these claims could be supported. The use of the word goal was unclear, ambiguous and misleading. The Panel ruled a breach of the Code as the claim that Zocor was the only statin licensed to reduce cholesterol, triglycerides and to raise HDL was inaccurate as Lipitor was also so licensed. The claim was different to the one at issue above as there was no reference to improved survival. The Panel considered that it was arguable as to the number of pages in the mailer. It might be considered to be eight pages or two pages folded up. On balance the Panel decided that the mailer consisted of two pages and therefore ruled no breach of the Code. The Panel noted that Parke Davis and Pfizer had misquoted the claim 'Zocor gets patients to goal at a lower price'. In the Panel's view the claim would be read as that the price of Zocor had been reduced. It would not been seen as a comparison with other statins as alleged by Parke Davis and Pfizer. No breach of the Code was ruled. It was clear in the mailing what was meant by the word goal. No breach of the Code was ruled.

Parke Davis and Pfizer alleged that the behaviour in relation to discussions prior to bringing the complaint to the Authority and the continued use of the misleading claim by Merck Sharp & Dohme had brought the pharmaceutical industry into disrepute and was in breach of Clause 2 of the Code. The Panel noted that the ABPI encouraged companies to discuss matter prior to bringing complaints to the Authority but there was no requirement to do so. The matter was not subject to the Code and the Panel made no ruling in this regard.

Parke Davis & Co Limited and Pfizer Limited complained about five promotional items for Zocor (simvastatin) issued by Merck Sharp & Dohme Limited. Parke Davis and Pfizer co-marketed Lipitor (atorvastatin). The items at issue were part of a promotional campaign which featured the claim 'Zocor enables up to 9 out of 10 CHD patients to reach the LDL-cholesterol goal of <3mmol/l'. The claim was considered first and then each promotional item individually.

1 Claim 'Zocor enables up to 9 out of 10 CHD patients to reach the LDL cholesterol goal of <3mmol/l'

COMPLAINT

Parke Davis and Pfizer stated that their fundamental concern regarding the claim was that it was highly misleading as the data cited by Merck Sharp & Dohme did not support it (alleged breaches of Clauses 7.3 and 7.8 of the Code); it was all embracing in nature (alleged breaches of Clauses 7.2 and 7.8); the wide body of data suggested the claim was false as there was more robust data available that contradicted the claim and showed that a physician could not reasonably expect that up to 9 out of 10 patients in a clinical practice would achieve the results promised (alleged breaches of Clauses 7.2 and 7.8).

Parke Davis and Pfizer alleged that the references cited by Merck Sharp & Dohme in support of the claim were misleading and not sufficient for a number of reasons.

The first reference, cited as data on file, supplied to Parke Davis and Pfizer on 8 September when supporting data for the claim was requested, was an abstract of data presented at the European Atherosclerosis Society meeting, 26 May 1999, Athens. The Pedersen study was a small study involving only 151 patients who suffered from acute coronary heart disease (CHD), which was only one sub-population of the CHD patients covered in the claim. Importantly, this reference only referred to simvastatin 40mg. Patients with acute CHD were known to have reduced LDL-cholesterol (LDL-C) levels secondary to the acute event. Thus the study population of patients had lower baseline LDL-C levels than normal, which made attainment of the stated goal easier to achieve than in the same population of patients without acute CHD. The Pedersen study did not include a broad enough range of CHD patients or patients at risk for CHD to support the claim. The study also failed to include any statistical analysis of patients getting to goal or reductions in LDL-C. This omission suggested that the data presented in the Pedersen study amounted to a post-hoc analysis of a study that was designed to examine other things. This omission of any statistical analysis, coupled with the small number of patients, also suggested that the data presented were not statistically significant.

The second reference provided by Merck Sharp & Dohme in support of the claim was a Parke Davis sponsored study, the Smith *et al* study (1999). Again the Smith study did not support the claim. It allowed for the concomitant use of cholestyramine with simvastatin in order to help patients reach the specified LDL-C target of 2.84mmol/l. Only 71% of the patients treated with simvastatin (10-40mg) monotherapy reached this target and even with cholestyramine, the figure was still only 80%. The use of cholestyramine was not mentioned anywhere in the Merck Sharp & Dohme promotional material and this was a different LDL-C goal than that referred to in the claim in any event. It was highly misleading to infer from that result that 'up to 9 out of 10' CHD patients reached target cholesterol levels of <3mmol/l for LDL-C and <5mmol/l for total cholesterol.

After objecting to Merck Sharp & Dohme that the data did not support the claim, Parke Davis and Pfizer were subsequently supplied with a reference regarding the Heart Protection Study (1999). This unpublished study was ongoing and involved treatment of CHD patients with simvastatin 40mg with placebo/antioxidant vitamins. Patients were also on a cholesterol lowering diet and other treatment to lower cholesterol (except for fibrates or niacin), which could include resins. More importantly, nowhere in this paper was there mention of patients achieving cholesterol targets.

As a result of the inadequacy of this data to support the claim, Parke Davis and Pfizer again contacted Merck Sharp & Dohme specifically requesting information from the Heart Protection Study that actually supported the claim. Merck Sharp & Dohme

stated that this information was sensitive and that the company was not prepared to provide this data. This failure to provide relevant information upon reasonable request was in itself a breach of Clauses 7.1 and 7.4 of the Code.

It was only after the Parke Davis again contacted Merck Sharp & Dohme, that this data was forthcoming, albeit two days later. This consisted of data on file derived from an interim analysis of the Heart Protection Study. It was insufficient to support any claim and detailed reasons were given. Parke Davis and Pfizer were also concerned that this data on file was a post-hoc analysis of a preliminary look at an on-going unpublished study that was conducted with selected patients using specifically the 40mg dose of simvastatin. The use of this data represented 'cherry picking' of the data and was not representative of the wider body of evidence for simvastatin. Accordingly the claim was not accurate, fair or balanced and was incapable of substantiation and therefore was in breach of Clauses 7.2 and 7.8 of the Code.

Parke Davis and Pfizer alleged that the use of the phrase 'up to' was highly misleading in that it suggested that up to and including 9 out of 10 patients in clinical practice could expect to achieve the specified cholesterol targets promised. As outlined above, the up to 9 out of 10 figure was not representative of what the clinician could reasonably expect from simvastatin and it therefore provided no reasonable guidance to the clinician and it could only mislead.

Although two of the studies cited by Merck Sharp & Dohme (the Heart Protection Study and the Pedersen study) involved only the use of the 40mg dose of simvastatin, the promotional materials and the claim failed to disclose that only this dose was used.

This lack of disclosure misled the practitioner into believing that simvastatin would achieve these results across all doses. The Zocor summary of product characteristics (SPC) stated that 20mg was the recommended starting dose for post-MI patients and otherwise that 10mg and 20mg were the recommended starting doses.

Simvastatin 10mg and 20mg were less effective than simvastatin 40mg at lowering LDL-C and Merck Sharp & Dohme was unwilling to provide evidence that up to 9 out of 10 patients in actual practice would achieve the results promised in the claim with these doses.

Accordingly, the claim was highly misleading and in breach of Clauses 7.2 and 7.8 of the Code.

Parke Davis and Pfizer stated that the Panel had previously ruled that a claim should be 'a balanced reflection of all the available evidence.' Other available published data on simvastatin suggested it was unlikely that up to 9 out of 10 patients taking simvastatin 10mg, 20mg, or even 40mg would achieve the promised results. Parke Davis and Pfizer referred to TARGET TANGIBLE trial (1999), Smith *et al* (1999), Dart *et al* (1997), Simons (1998) and AAA (1999). For example:

- In the TARGET TANGIBLE trial, overall only 53% of simvastatin (10-40mg) treated patients achieved a LDL-C target of ≤2.6mmol/l.
- In the Smith study, only 71% of the patients treated with simvastatin (10-40mg) monotherapy reached the target of 2.6mmol/l and even with cholestyramine, the figure was still only 80%.
- The study by Dart showed that only 27% of patients treated with simvastatin 10mg achieved LDL-C target of <3.36mmol/l.
- The Simons study showed that only 6% of patients treated with simvastatin 40mg (plus 4g cholestyramine in 84% of the patients by study end) achieved LDL-C target of <3.5mmol/l and just 26% of these patients achieved a less aggressive goal of <4.5mmol/l.
- In a treat to target study (AAA), overall 65.9% of patients achieved a total cholesterol target of <5.0mmol/l on simvastatin 10-40mg, (plus 4g cholestyramine in some patients), after 24 weeks.

These data therefore illustrated that the claim was not reflective of the efficacy of simvastatin demonstrated in the wider body of published studies and therefore was in breach of Clauses 7.2 and 7.8.

RESPONSE

Merck Sharp & Dohme submitted that reaching a target cholesterol level in patients with confirmed CHD was becoming of increasing importance in primary care. The National Service Framework (NSF) for CHD care was likely to recommend that patients with CHD had their LDL-C level reduced to below 3mmol/l in line with recommendations published earlier in 1999 (Joint British recommendations on prevention of coronary heart disease in clinical practice). It was important to communicate this message to primary care physicians in particular, and to outline what they could expect in this regard from simvastatin in typical CHD patients.

Despite the fact that reaching goal cholesterol levels was being given increasing prominence by government, there was a paucity of data on statin treatment in general looking at the specific question of how many patients could reach the goal of LDL-C <3mmol/l in a typical CHD population. Simvastatin had data on this specific question, as outlined in the Pedersen study quoted in the promotional material.

This study was criticised by Parke Davis and Pfizer at a variety of levels which Merck Sharp & Dohme regarded as unfounded. The numbers of patients in the study were quite in line with data quoted in promotional material elsewhere. Indeed Parke Davis and Pfizer quote a paper by Nawrocki *et al* in several of their promotional items which included only 57 patients.

The abstract demonstrated that 90% of patients reached goal if treated immediately with simvastatin 40mg when in hospital with an acute ischaemic event. The result was significant at 3 months compared to those patients treated with diet alone – this was implied in the abstract though not actually stated.

Merck Sharp & Dohme stated that the point made by Parke Davis and Pfizer as regards the baseline cholesterol of these patients being artificially low was irrelevant. It was increasingly standard practice to

treat patients with statins immediately after their ischaemic event and therefore the response in the immediate treatment group reflected what would be expected in usual care. Also any temporary effect on LDL-C of the patient's myocardial infarction would have resolved at 6 months and yet 90% of patients were still within goal at this time.

Other papers quoted in this piece were simply designed to demonstrate that lower doses of simvastatin than 40mg could also get many patients to goal. The Smith paper demonstrated this – 35% of patients in this study achieved a goal LDL of 2.6mmol/l with 10mg of simvastatin. Merck Sharp & Dohme appreciated that this was not the goal mentioned in the advertisement but it was a lower one and still illustrated the principle very effectively. The paper did not allow the number of patients who would reach the higher LDL goal of 3mmol/l on 40mg daily of simvastatin to be guessed, but that was not what was being demonstrated by using this reference.

It was clear that it was the highest dose of simvastatin (40mg) which would achieve a goal most frequently, but, as had been stated, lower doses would do it in many people. It was this point which was being made by the term 'up to' ie 9 out of 10 was what would be expected at 40mg but at doses 'up to' that lower numbers would reach goal – clearly doctors would not need to use 40mg simvastatin if lesser doses could achieve goal in their individual patient.

The complainants had quoted several papers which had suggested that these showed the claim for 9 out of 10 CHD patients achieving a goal LDL-C of <3mmol/l with 40mg to be misleading. Merck Sharp & Dohme stated that unfortunately none of these references supported that suggestion.

– The TARGET TANGIBLE Trial used a lower cholesterol goal of 2.6mmol/l so it was not possible to state from this paper what percentage would have reached goal if the target had been higher. This also applied to the Smith study as had been stated.

– The Dart study was in hypercholesterolaemic patients (mean total cholesterol 7.34mmol/l) which was hardly representative of the CHD population in which the claim was made. Also this study did not use 40mg simvastatin.

– The Simons study similarly was in severe primary hypercholesterolaemia, again not in any way representative of the CHD population to which the advertisement alluded.

– The treat to target study (AAA) quoted by Parke Davis and Pfizer was very interesting. The body of the population studied was more severely hypercholesterolaemic, again not representative of the CHD patients to which the advertisement referred. However if one looked at the sub-group of the population whose baseline total cholesterol better reflected that of CHD patients (5.2-6.5mmol/l) it could be seen that 87% reached a target of total cholesterol of <5mmol/l (roughly equivalent to an LDL-C of 3mmol/l) on simvastatin at doses up to 40mg, which supported the claim very well.

In contrast to the highly unusual study populations described in the studies quoted by Parke Davis and Pfizer, the patients in the Pedersen study had cholesterol levels which reflected very well those found in a UK CHD population. Merck Sharp & Dohme provided confidential data regarding the average total cholesterol in a population of almost 10,000 untreated CHD patients (the Healthwise database).

Merck Sharp & Dohme submitted that there was thus no data available to contradict the claim that up to 9 out of 10 patients with CHD could achieve a goal LDL-C <3mmol/l with Zocor. This claim was supported by the data referenced, was not all embracing, misleading or unfair and was substantiated by the evidence so far available. The company denied breaches of Clauses 7.2, 7.3 and 7.8.

As regards the alleged breaches of Clauses 7.1 and 7.4, Merck Sharp & Dohme submitted that there was no case to defend. Information from the Heart Protection Study was provided to Parke Davis and Pfizer in confidence when they complained about the advertisement. This data was a confidential interim analysis which further supported the 9 out of 10 claim. However it was not intended to be used in promotion at this stage, it had not been referenced in defence of the claim and Merck Sharp & Dohme was under no obligation to provide it as the medical information department quite rightly explained. The company was quite happy that the references used in the advertisement supported the claim.

Breaches of Clauses 7.1 and 7.4 were denied and Merck Sharp & Dohme added that it might have been more reluctant to submit this confidential data to Parke Davis and Pfizer in good faith, had it known that the data would in part form the basis of complaint.

PANEL RULING

The Panel noted that the claim for Zocor that 'up to 9 out of 10 CHD patients can reach the LDL-C goal of <3mmol/l' had been complained about in two earlier cases, Case AUTH/937/10/99 and Case AUTH/941/10/99.

The Panel noted that in Case AUTH/937/10/99, the claim was attributed to Pedersen, European Atherosclerosis Society, Athens May 1999. The claim was followed by an obelus which referred to new joint recommendations from the British Cardiac Society, the British Hyperlipidaemia Association and the British Hypertension Society (endorsed by the British Diabetic Association) of total cholesterol <5mmol/l and LDL-C <3mmol/l.

Merck Sharp & Dohme provided data to support the claim. Pedersen *et al* (1999) was an abstract reporting a study carried out in patients with acute myocardial infarction (n=112) or unstable angina (n=39) and LDL-C ≥3mmol/l who were allocated to one of two strategies of lipid intervention. Both groups had dietary counselling, one group received simvastatin 40mg daily from the day of randomisation whilst the other started simvastatin after 3 months if LDL-C was still ≥ 3mmol/l. At six months 82% of patients in the deferred treatment group had reached target. 90% of patients in the immediate treatment group had

reached target after 3 months and remained on target at six months.

A study by Giles *et al* (1998) showed that 83% of post myocardial infarct patients achieved a total cholesterol of less than 5.2mmol/l. The mean total cholesterol at entry was 5.97mmol/l. The choice of lipid lowering medication depended on the triglyceride level but in practice the overwhelming majority of patients were treated with simvastatin at a dose of 10mg daily. Merck Sharp & Dohme had undertaken a subgroup analysis of 229 patients who had been so treated. This analysis was presented as data on file and showed that 10mg of simvastatin achieved the stated LDL-C target of 3mmol/l in 75% of patients and total cholesterol target of 5mmol/l in 72% of patients. It was not stated what sub-group had been analysed or how it had been identified. Nor was it stated at what time point the assessment was made.

The Panel noted the information from the Heart Protection Study (1999) which was being carried out on patients who were considered to be at elevated risk of coronary heart disease death because of past history.

The Panel considered that overall the data were not sufficient to support the claim 'up to 9 out of 10 CHD patients can reach the LDL-C goal of <3mmol/l'. The Pedersen study supported the claim but only for a 40mg dose of Zocor. Data on file from the Giles study (Zocor 10mg) and the Heart Protection Study (Zocor 40mg) lacked sufficient detail to allow the clinical significance of either to be assessed. In addition the Panel considered that the claim '9 out of 10' would be read as applying to all doses of Zocor; the use of the words 'up to' were not enough to correct this misleading impression. Overall the Panel considered that the claim was misleading, exaggerated and not capable of substantiation. The Panel ruled breaches of Clauses 7.2, 7.3 and 7.8 of the Code.

Turning to the case now before it, the Panel decided that its rulings in Case AUTH/937/10/99 of breaches of Clauses 7.2, 7.3 and 7.8 would also apply here. In addition the Panel ruled a breach of Clause 7.4 of the Code as substantiation had not been provided. The Panel considered that its ruling of a breach of Clause 7.4 covered the allegation of a breach of Clause 7.1.

2 Separate allegations were made about a number of promotional items

a) Journal advertisement (ref 08-00ZCR.99. GB.70159.j.b. (September 1999))

The advertisement included the claim 'Zocor – proven efficacy up to 9 out of 10 CHD patients can reach the LDL-C goal of <3mmol/l'.

COMPLAINT

Parke Davis and Pfizer alleged that the claim was in breach of Clauses 7.2, 7.3 and 7.8 for the reasons in point 1 above. It was also misleading as it did not clearly disclose the dose of Zocor required to achieve the stated goal. The impression given was that the claim related to all the licensed doses of Zocor.

RESPONSE

Merck Sharp & Dohme submitted that as outlined above there was no evidence available to indicate this was untrue in a typical CHD population and for reaching this particular goal. Many CHD patients reached goal on lower doses than the top dose of 40mg but 9 out of 10 would reach goal if simvastatin was used through its full dose range.

PANEL RULING

The Panel decided that its rulings of breaches of Clauses 7.2, 7.3 and 7.8 in point 1 above would also apply here.

b) Price Reduction Letter (ref 10-00 ZCR.99. GB.10333.7m.QO.1099)

The price reduction letter referred to changes in price for Zoton and to features of the medicine.

The letter had been the subject of another complaint (Case AUTH/941/10/99) when Merck Sharp & Dohme advised that the letter had been sent to chief executives, medical advisers, pharmaceutical advisers and directors of public health as well as to primary care group personnel.

COMPLAINT

Parke Davis and Pfizer alleged that the claim 'Zocor can deliver up to 9 out of 10 patients to the target cholesterol levels outlined in the new Joint British Recommendations for Coronary Heart Disease and many patients will achieve target levels using the 10mg stating dose' was in breach of Clauses 7.2, 7.3 and 7.8 of the Code for the reasons stated in point 1 above.

Parke Davis and Pfizer alleged that the claim 'Zocor is the only statin licensed to reduce cholesterol, triglycerides and to raise HDL-Cholesterol' was a factually incorrect exaggeration that was misleading. Lipitor (atorvastatin) was licensed to reduce cholesterol and triglycerides and, as of 24 September 1999, to raise HDL-Cholesterol.

The updated Lipitor SPC was available on 24 September on RAMA, the MCA database, to which Merck Sharp & Dohme subscribed. The date of preparation of this letter was 1 October. Therefore it was apparent that Merck Sharp & Dohme did not make any reasonable attempts to ensure that the claim was correct and continued promoting it after 5 October. It was only on 5 October, that Parke Davis received a request for a copy of the updated SPC, which was forwarded by fax. Thus the particular claim was in breach of Clauses 7.2 and 7.8 of the Code.

Parke Davis and Pfizer alleged that the prescribing information on the reverse of this letter was also incorrect. The letter highlighted new lower prices for Zocor whilst the prescribing information continued to refer to the old prices and was thus misleading. A breach of Clause 7.2 of the Code was alleged.

The letter also claimed that 'Zocor offers unique benefits to the NHS and patients through its

unsurpassed survival data, efficacy across all lipid parameters, proven long-term tolerability and cost-effectiveness data.' The use of the word 'unique' implied exclusivity and was misleading as simvastatin was not the only statin to be effective across all lipid parameters, proven to be well tolerated or to have cost-effectiveness data. This was therefore a breach of Clause 7.8 of the Code, as these were not defined special features of simvastatin. It implied a general superiority for simvastatin that was misleading and a breach of Clause 7.2 of the Code was also alleged.

RESPONSE

Merck Sharp & Dohme referred to its response to point 1 above.

Merck Sharp & Dohme accepted that an inadvertent breach of the Code occurred, in that the claim that Zocor was the only statin licensed to raise HDL-C was made after atorvastatin had acquired this licence on 24 September. Merck Sharp & Dohme was disappointed that Parke Davis and Pfizer complained formally about this, since it had already agreed to withdraw this promotion and had accepted the inadvertent breach. Merck Sharp & Dohme stated that it had been making that particular claim for many months prior to the atorvastatin licence change and Parke Davis and Pfizer were well aware of this fact. Merck Sharp & Dohme would have hoped that during the many intercompany discussions over recent weeks it could have been alerted to this change – after all, the purpose of intercompany dialogue was to avoid unnecessary complaints being made.

Merck Sharp & Dohme accepted the breach of the Code concerning the prescribing information – this had been corrected.

Merck Sharp & Dohme submitted that Zocor was unique in that it provided unsurpassed survival data (only pravastatin and simvastatin had data showing survival advantage), efficacy across all lipid parameters (only simvastatin and atorvastatin were licensed to raise HDL-C) and had more long term safety data than any other statin. This broad range of features was unique to simvastatin and therefore the claim was qualified and justified. Merck Sharp & Dohme therefore rejected breaches of Clauses 7.2 and 7.8.

PANEL RULING

The Panel noted the '9 out of 10' claim at issue was similar to the claim in point 1 above. The claim had also been the subject of a previous case, Case AUTH/941/10/99. The Panel considered that its rulings of breaches of Clauses 7.2, 7.3 and 7.8 in point 1 above also applied here.

The Panel noted that Parke Davis and Pfizer had only quoted part of the claim 'Zocor is also the only statin licensed to improve survival, lower cholesterol, triglycerides and raise HDL – Cholesterol'. The complainants had omitted the reference to improving survival. The Panel noted that the licence for Lipitor had been amended to include raising HDL-C. Lipitor was not licensed to improve survival. Only Zocor and pravastatin were so licensed. Pravastatin was not licensed to raise HDL-C. Zocor was the only statin licensed for the four features given in the claim. The Panel considered that the claim was not unacceptable and no breach of Clauses 7.2 and 7.8 of the Code were ruled.

The Panel noted that the letter itself clearly gave the old prices for Zocor, the new price and the percentage price reduction. The prescribing information, included on the reverse of the letter, gave the old price. The Panel noted that guidance had been issued in the August 1999 Code of Practice Review with regard to price reductions as a result of the revised Pharmaceutical Price Regulation Scheme. The guidance stated that in the period 1 October to 31 December promotional material would not be considered to be in breach of the Code if it still carried the previous higher price. The Panel considered that the letter was covered by the guidance. Readers would be clear about the price changes. No breach of Clause 7.2 of the Code was ruled.

The Panel noted that it had already ruled on the use of 'unique' in an earlier case, Case AUTH/941/10/99. In the earlier case the Panel noted the supplementary information to Clause 7.8 stated that great care needed to be taken with the use of the word unique. It might be used to describe some clearly defined special feature of a medicine. Its use to imply a general superiority was not possible to substantiate. The Panel considered that the word unique was used to imply a general superiority and this implied that Zocor had some special merit which could not be substantiated. Breaches of Clauses 7.2 and 7.8 were ruled.

The Panel considered that its rulings of breaches of Clauses 7.2 and 7.8 of the Code in the earlier case also applied here.

c) Journal advertisement (ref 08-00ZCR.99. GB.70159.J.D.)

The '9 out of 10' claim had been amended to read 'Zocor – proven efficacy up to* 9 out of 10 CHD patients can reach the LDL-C goal of <3mmol/l'. The asterisk was explained as 'Using recommended daily dose range 10-40mg'. The explanation appeared beneath the 9 out of 10 claim and before the 'CHD patients can achieve the LDL-C goal of 3<mmol/l.

COMPLAINT

Parke Davis and Pfizer stated that although the claim now included reference to the dosage range of 10-40mg, this still did not clearly define the dosage of simvastatin required to achieve the defined therapeutic goal.

In fact, the claim now implied that simvastatin 10mg achieved the goal in up to 9 out of 10 patients which was factually incorrect and therefore misleading to prescribers. It was alleged that this revised advertisement was in breach of Clauses 7.2, 7.3 and 7.8 of the Code.

RESPONSE

Merck Sharp & Dohme stated that following representations from Parke Davis and Pfizer at a meeting on 16 September 1999, it undertook to review the first '9 out of 10' advertisement in light of their comments. This was done in a spirit of co-operation and in order to avoid unnecessary referral to the Authority. Merck Sharp & Dohme did not accept their criticisms of the initial advertisement or of its data.

Within the new advertisement, developed as a result of this consultation process, the dosage range for Zocor was included to highlight to clinicians that 'up to' referred to the fact that the proportion of CHD patients reaching the goal depended on the dose given, but again that by the time the doctor had titrated to 40mg, '9 out of 10' CHD patients would have reached goal.

Merck Sharp & Dohme in no way accepted that this modification now implied that 10mg simvastatin achieved goal in '9 out of 10' patients as Parke Davis and Pfizer had tried to suggest. The claim for '9 out of 10' reaching goal was for the brand as a whole within its dose range. Many patients did reach goal on 10mg and for them further titration upwards of the dose was unnecessary. By this promotion Merck Sharp & Dohme was seeking to reassure clinicians that for those patients who did not achieve goal on lower doses, higher doses would work in the vast majority of CHD patients if they persevered with dosage increases.

Merck Sharp & Dohme therefore rejected the alleged breach of Clauses 7.2, 7.3 and 7.8 of the Code.

PANEL RULING

The Panel noted that the claim was a slightly amended version of that at issue in points 1 and 2a above.

The Panel considered that the addition of the asterisk and the explanation 'using recommended daily dose range 10-40mg' was not adequate. The claim would be read as applying to doses of 10mg as well as 40mg. The Panel considered that its rulings of breaches of Clauses 7.2, 7.3 and 7.8 of the Code in point 1 also applied here.

d) Journal advertisement (ref 10-00ZCR.99. GB.70259.J.b. (October 1999))

The advertisement included the claim

'Zocor – proven efficacy up to* 9 out of 10'

- CHD patients reach the LDL-C goal of <3mmol/l.
- Many patients will reach <3mmol/l at starting doses.

The explanation for the asterisk was the same as in point 2c above and appeared in a similar position.

COMPLAINT

Parke Davis and Pfizer alleged that this version of the advertisement was still misleading and in breach of Clauses 7.2 and 7.8 of the Code for the same reasons outlined in 2(c) above. When asked to provide evidence supporting the 'up to 9 out of 10' for the 10mg and 20mg doses of simvastatin, Merck Sharp & Dohme declined to do so on the basis that it was not necessary to provide substantiation for the claim at specific doses of simvastatin. A breach of Clause 7.4 of the Code was alleged.

RESPONSE

Merck Sharp & Dohme stated that following further representations from Parke Davis and Pfizer a second revision to the advertisement was made. It re-iterated that these alterations should not prejudice how earlier versions were viewed with respect to adherence to the Code. Merck Sharp & Dohme took the obligation for companies to try and resolve issues without reference to the Authority very seriously, and this further alteration was again made to try and satisfy the concerns of Parke Davis and Pfizer. With hindsight and having reviewed the complaint, this might have been optimistic.

Merck Sharp & Dohme stated that it added the strap line that 'Many patients will reach <3mmol/l at starting doses' to further emphasise the points made in 2c above. Yet again it did not consider that this alteration was necessary but was willing to make it to maintain good intercompany relations. For the reasons already outlined, breaches of Clauses 7.2 and 7.8 of the Code were denied.

Merck Sharp & Dohme stated that Parke Davis and Pfizer requested data supporting 9 out of 10 CHD patients reaching goal on 10mg and 20mg doses of simvastatin. The fact that these were not provided led to the alleged breach of Clause 7.4. The advertisement did not claim that these doses reached goal in 9 out of 10 CHD patients. The complaint was misconceived and Merck Sharp & Dohme could not be expected to provide references which supported misinterpretations of the claim.

PANEL RULING

The Panel noted that the claim was a slightly amended version of those at issue in points 1, 2a and 2c above.

The Panel considered that the slight change in layout and the addition of the claim 'many patients will reach <3mmol/l at starting doses' was not adequate. The claim as a whole would be read as applying to doses of 10mg as well as 40mg and that the impression was that 9 out of 10 patients would reach <3mmol/l at 10mg dose. There was not sufficient data to support that impression. The Panel considered that its rulings of breaches of Clauses 7.2, 7.3 and 7.8 in point 1 also applied here. The Panel noted that the data did not support the claim and therefore ruled a breach of Clause 7.4 of the Code.

e) Zocor Mailer (ref 10-00ZCR.99. GB.70269.M.57m.QO.1099 (October 1999))

The mailer consisted of 4 circles printed on both sides joined together at the edge of each of the four circles.

The mailing was folded concertina like to the size of one circle. The first circle bore the photograph of the reverse side of a £1 coin and the second circle bore the photograph of the reverse side of a £2 coin. Superimposed on the third circle which also bore the photograph of the reverse side of a £1 coin was the claim 'Zocor now gets patients to goal at lower price'. The mailer included the claims 'Up to* 9 out of 10 CHD patients can achieve the LDL-C goal† when treated with Zocor' and 'Zocor proven efficacy up to* 9 out of 10'. The item also included the claim 'The only statin licensed to reduce cholesterol, triglycerides and to raise HDL'. It referred to the reduced cost of Zocor.

COMPLAINT

Parke Davis and Pfizer stated that the mailer was sent to doctors on 4 October. Parke Davis alleged that the 'up to 9 out of 10' claim was in breach as outlined in point 1 above.

Parke Davis and Pfizer alleged that the claim 'The only statin licensed to reduce cholesterol, triglycerides and to raise HDL' was in breach of Clauses 7.2, 7.3 and 7.8 of the Code as outlined in point 2b above.

The mailer consisted of more than four pages and there was no indication as to where the prescribing information could be found. A breach of Clause 4.6 of the Code was alleged.

The claim 'Zocor now gets more patients to goal at a lower price' was alleged to be all-embracing and also a hanging comparison. It suggested that simvastatin got more patients to their goal than any other statin and that simvastatin got more patients to their goal more cheaply than with any other statin. Neither of these claims could be supported. The claim was not supported by the Smith study which concluded, 'In patients with CHD and/or peripheral vascular disease, LDL-C target is achieved faster using fewer resources and at a significant cost saving with atorvastatin compared with fluvastatin, pravastatin or simvastatin'. In addition the word 'goal' did not specify whether it related to lowering cholesterol or any other type of goal that the prescriber might choose to address. As such the claim was unclear, ambiguous and misleading and therefore in breach of Clauses 7.2, 7.3 and 7.8 of the Code.

RESPONSE

Merck Sharp & Dohme rejected the allegation that the '9 out of 10' claims were in breach of Clauses 7.2, 7.3 and 7.8 of the Code.

With regard to the claim concerning HDL-C, Merck Sharp & Dohme accepted that this was an inadvertent breach of the Code but it was satisfied that as a company it took all reasonable steps to avoid such errors. In these situations all companies had to rely to some extent on the goodwill of their competitors to alert them to licence changes.

With regard to the alleged breach of Clause 4.6 Merck Sharp & Dohme explained that the item was designed to unfold completely such that one side could be read in its entirety from top to bottom. The reverse side had the prescribing information on it. It was viewed as a two-sided item which did not require a reference as to where the prescribing information was located.

Merck Sharp & Dohme stated that Parke Davis and Pfizer had misquoted the claim 'Zocor now gets patients to goal at a lower price'. The claim did not use the word 'more' as stated by the complainants. Merck Sharp & Dohme submitted that a comparison was only hanging if it was not clear what the comparison was with and here that was not so. It was clear that the claim meant that Zocor was now less expensive than it was previously. Such language was in common use in promotion and few people, if any, could misinterpret this. To draw an analogy, if brand name jeans were advertised as being 'now at a lower price' it would not be conceivable that they would be viewed as the cheapest jeans in the country. In addition Parke Davis and Pfizer had stated that the word 'goal' was not defined. Merck Sharp & Dohme submitted that most clinicians were well aware of cholesterol goals and would understand this. The term was very well explained within the mailer. Merck Sharp & Dohme rejected the allegation that the claim was in breach of Clauses 7.2, 7.3 and 7.8 of the Code.

PANEL RULING

The Panel decided that with regard to the claim 'Up to 9 out of 10…' its ruling of breaches of clauses 7.2, 7.3 and 7.8 in point 1 above would also apply here.

The Panel ruled that the claim that Zocor was the only statin licensed to reduce cholesterol, triglycerides and to raise HDL was inaccurate as Lipitor was also so licensed. A breach of Clause 7.2 of the Code was ruled. The claim was different to the one at issue in point 2b above as there was no reference to improved survival.

The Panel considered that it was arguable as to the number of pages in the mailer. It might be considered to be eight pages or two pages folded up. On balance the Panel decided that the mailer consisted of two pages and therefore ruled no breach of Clause 4.6 of the Code.

The Panel noted that Parke Davis and Pfizer had misquoted the claim 'Zocor gets patients to goal at a lower price'. In the Panel's view the claim would be read as that the price of Zocor had been reduced. It would not be seen as a comparison with other statins as alleged by Parke Davis and Pfizer. No breach of Clauses 7.2, 7.3 and 7.8 of the Code were ruled.

The Panel considered that the use of the word goal was not unclear, misleading or ambiguous. It was clear in the mailing what was meant by the word 'goal'. No breach of Clauses 7.2, 7.3 and 7.8 was ruled.

3 Conduct of Merck Sharp & Dohme

COMPLAINT

Parke Davis and Pfizer stated that in keeping with the spirit of the Code, they had tried to address their concerns with Merck Sharp & Dohme without

recourse to the Authority. On a number of occasions the companies considered that agreement had been reached only to find that Merck Sharp & Dohme had then breached the agreement or was seeking to circumvent the agreement by use of new materials carrying the same misleading claims. A summary of the attempts to resolve this matter informally was provided. Parke Davis and Pfizer alleged that this behaviour and the continued use of the misleading claim by Merck Sharp & Dohme had brought the pharmaceutical industry into disrepute and was in breach of Clause 2 of the Code.

RESPONSE

Merck Sharp & Dohme accepted that in a highly competitive environment companies would take issue with each other's promotion on a variety of fronts.

The assertions Parke Davis and Pfizer made with regard to the alleged breach of agreements were wholly without substance or foundation. At no point in either written, verbal or electronic communication had Merck Sharp & Dohme stated that it would stop making the '9 out of 10' claim in toto. The only item it had ever agreed to modify was the initial advertisement.

Merck Sharp & Dohme was surprised that Parke Davis and Pfizer had chosen to bring these intercompany discussions into the public arena in this manner in alleging a breach of Clause 2. Merck Sharp & Dohme disagreed with their interpretation of events. Merck Sharp & Dohme rejected utterly any suggestion that in this dispute it had breached Clause 2 of the Code. Its actions had been made entirely with a view to maintaining good relations between companies.

PANEL RULING

The noted that Parke Davis and Pfizer had alleged a breach of Clause 2 of the Code in relation to matters discussed between the companies prior to the complaint being made.

The ABPI encouraged companies to discuss matter prior to bringing complaints to the Authority but there was no requirement to do so. The matter was not subject to the Code and the Panel made no ruling in this regard.

Complaint received **2 November 1999**

Case completed **6 January 2000**

CASE AUTH/952/11/99

PHARMACEUTICAL ADVISOR v FERRING

Pentasa mailing

A pharmaceutical advisor to a primary care group wrote to Ferring to complain about a Pentasa (mesalazine SR) mailing and copied the letter of complaint to the Authority. The mailing informed readers that if they prescribed Pentasa, instead of the current most commonly prescribed mesalazine brand, they could help the NHS save £6 million. The mailing stated that with £6 million the NHS could fund, *inter alia*, an additional 1,000 coronary bypass procedures. The complainant presumed that the implied link between saving £6 million and prescribing Pentasa was a spoof and considered that it was neither honest nor truthful. Such a simplistic attempt to hoodwink prescribers was unlikely to succeed and brought Ferring, and thus Pentasa, into disrepute.

The Panel noted that the projected saving was based solely on drug acquisition costs over one year, although the time scale was not given in the mailing. In the Panel's view, for this saving in the drug's budget to be realised then the efficacy and tolerability of Pentasa and the more commonly prescribed mesalazine brand would have to be equivalent. The mailing assumed that the projected saving in the drug's budget would be wholly available for use elsewhere in the NHS which might not be the case. Additionally, the Panel considered that although the mailing stated that the average cost to the NHS of a coronary bypass procedure was £5,673, this did not mean that an additional £6 million would fund an additional 1,000 such procedures as current staff and resources might not have the capacity to cope with the extra load. The Panel considered that the mailing oversimplified funding issues in the NHS. The claims were misleading and could not be substantiated. Breaches of the Code were ruled. The Panel did not consider that the mailing was such as to offend recipients or bring discredit upon the company or the pharmaceutical industry as a whole and no breach of the Code was ruled in that regard.

A pharmaceutical advisor to a primary care group (PCG) wrote to Ferring Pharmaceuticals Ltd to complain about a Pentasa (mesalazine SR) mailing (ref G/47/10/99) which it had sent to one of the GPs in the PCG. The letter of complaint was copied to the Authority. The mailing in question had four square flaps positioned around a central square so that when fully unfolded it formed the shape of a cross. The folded up mailing started by stating 'You could help the NHS save £6,000,000'. As the mailing was unfolded four examples of what the NHS could fund with £6 million were shown ie an additional 1,000 coronary bypass procedures, an additional 1,300 elective primary knee replacements, an additional 1,600 elective primary hip replacements or successful drug treatment for 1,600 infertile patients. The mailing stated that the way to help save the NHS £6m was to 'Simply prescribe Pentasa (mesalazine) Slow Release Tablets 500mg. Based on 1998 NHS usage, an average Pentasa prescription now costs 29% less than the current most commonly prescribed mesalazine brand'.

The mailing was sent to consultant gastroenterologists, colorectal surgeons, senior registrars, PCG lead GPs, practice managers and hospital pharmacists.

COMPLAINT

The complainant presumed that the implied link between saving £6 million and brand prescribing of Pentasa was a spoof.

The complainant noted that the current most commonly prescribed brand of mesalazine was presumably Asacol, which was a 400mg preparation anyway so a switch would not be appropriate. On the brand prescribing question, there did not seem to be any generics available at present though, of course, Ferring might have knowledge of a future change.

The complainant considered most strongly that that attempt to link Pentasa with a saving of £6 million (over what time-scale?) was neither honest nor truthful. Such a simplistic attempt at hoodwinking prescribers was unlikely to succeed and simply brought Ferring, and thus Pentasa, into disrepute.

RESPONSE

Ferring stated that the mailing was a follow-up mailer intended to highlight the cost savings that could be achieved by the NHS through the wider use of Pentasa 500mg. The background to this was a price reduction of 20% from £32.28 to £25.82 with effect from 1 October, which had previously been publicised in the media and by earlier mailings, which also highlighted a 29% cost difference between Pentasa 500mg and the current most commonly prescribed brand.

The mailing was based on conservative estimates following the price reduction of Pentasa 500mg and the £6 million NHS saving referred to could realistically be achieved through wider use of Pentasa 500mg. This was because the cost of an average prescription of Pentasa was now 29% less expensive than the current most commonly prescribed brand of mesalazine 400mg tablets.

Ferring stated that according to the 1998 Prescription Cost Analysis for England, the NHS spent over £24 million on mesalazine 400mg tablets; this inferred that at least 34,000 patients were so treated. Extrapolating these results to include the rest of the UK gave an estimated NHS spend in excess of £28 million for mesalazine 400mg tablets, which represented a patient base of at least 39,800, even assuming continuous treatment. This figure was also supported by IMS published figures of over £28.5 million. In their 1996 guidelines, the British Society of Gastroenterology suggested that there were about 80,000 ulcerative colitis sufferers in the UK and Rubin *et al* (1996) estimated that there might be as many as 135,000 such patients.

Ferring submitted that to achieve an annual NHS cost reduction of £6 million it would be necessary to treat approximately 29,000 patients with Pentasa 500mg instead of the current most commonly prescribed brand. Therefore, the saving of £6 million would be achieved through a switch of approximately two thirds from the current most commonly prescribed brand to Pentasa and the company considered that this goal was attainable given the 29% cost advantage.

In addition to this, the 20% cost reduction in Pentasa 500mg would already result in an annual NHS cost saving of over £500,000 for those patients currently treated with Pentasa.

Ferring noted that the complainant contended that it would not be appropriate to switch patients from the 400mg enteric coated tablets to Pentasa 500mg. This was not supported by current clinical practice and this point of view was supported by a professor of gastroenterology who was one of the leading authorities on inflammatory bowel disease in the UK.

Ferring stated that although there were few direct comparisons published, each brand of mesalazine had demonstrated equivalent efficacy to sulphasalazine and there was no evidence that, for the treatment of ulcerative colitis, any one brand offered significantly better efficacy than another. Experience from many countries suggested that the first brand on the market usually enjoyed the largest share of that market and there was inertia to change unless there was a good reason, such as clinical superiority or a significant price advantage.

Ferring stated that the normal daily dose of mesalazine was 1.2g to 4g divided into two to four doses. If mesalazine 400mg enteric coated tablets were used, then the dose regimen was based on multiples of 400mg and if Pentasa 500mg were prescribed, the dose was based on multiples of 500mg. The effects of the two products were broadly similar, although the unique slow release formulation of Pentasa conferred the advantage of a consistent continuous release of mesalazine coupled with low blood levels in comparison with alternative formulations. This might have safety implications as discussed by the professor of gastroenterology in his letter, although there was no definitive conclusion and the company did not, therefore, raise this as a concern in this promotion.

The 1998 Prescription Cost Analysis showed that the average number of tablets per prescription was similar for both products and this inferred a daily dose of 5 to 6 tablets daily for either mesalazine 400mg enteric coated tablets or for Pentasa 500mg. Based on this, the average annual cost of treating a patient with mesalazine 400mg was about £703 whereas the cost of treating with Pentasa 500mg would be about £497. In other words, the difference in cost between these two alternatives would on average be of the order of £206 (29%) per patient per year of treatment.

Ferring accepted that not all patients were suitable for treatment with mesalazine and that for some the choice of formulation would be important. In using oral mesalazine to treat ulcerative colitis, the dose was set from the formulation chosen, but for many patients Pentasa 500mg was a viable choice of treatment, which now offered a significant price advantage over the current most commonly prescribed brand.

Ferring stated that it had discussed these issues in some detail with the complainant and he accepted that there was merit in the company's assessment that Pentasa 500mg could be an appropriate alternative to mesalazine 400mg tablets for suitable patients. The complainant had also expressed interest in the potential cost saving that Pentasa could offer and requested further information because he did not recall reading the first mailer.

With regard to each clause of the Code which it had been asked to consider, Ferring made the following comments:

Clause 2: The company was highlighting the substantial cost differential between Pentasa and the current most commonly prescribed brand of mesalazine. For the vast majority of patients Pentasa 500mg represented an entirely appropriate choice of therapy. The promotion was based on evidence which could be substantiated and there was no attempt to mislead prescribers or to discredit competitors.

Clause 7.2: The company had used the latest available information and had not made any unrealistic assumptions in calculating the financial benefits of prescribing Pentasa instead of the current most commonly prescribed brand; the company had not suggested that Pentasa was necessarily the best treatment for all patients. However, Ferring considered that there was adequate information to support Pentasa tablets as an appropriate choice for the vast majority of patients and that being first on the market was a major factor in determining the leading brand. There were, therefore, no misleading claims as part of this promotion.

Clause 7.3: The company considered that it had substantiated the claims made in this promotion.

Clause 9.1: Ferring stated that it was surprised by the tone of the complainant's letter and given that it could substantiate the claims made, it did not believe that this promotion was likely to cause offence. After discussing the matter with the complainant, he was reassured by the evidence that substantiated the claims made in this promotion.

PANEL RULING

The Panel noted that six million pounds was the annual projected saving which would be achieved through the use of Pentasa 500mg instead of mesalazine 400mg tablets; the time scale was not given in the mailing. The projected saving was based solely on drug acquisition costs. In the Panel's view, for this saving in the drug's budget to be realised, then the efficacy and tolerability of Pentasa and mesalazine 400mg tablets would have to be equivalent.

The mailing assumed that a six million pound annual saving in the drug's budget would be wholly available for use elsewhere in the NHS. In the Panel's view this might not be the case. Additionally the

Panel considered that although the mailing stated the average cost to the NHS of a coronary bypass procedure was £5,673, this did not mean that an additional £6m would fund an additional 1,000 such procedures. Inherent in such a claim was the assumption that current nursing and medical staff, and resources such as hospital beds and operating theatres, had the capacity to cope with 1,000 additional coronary artery bypass operations. This might not be the case.

The Panel considered that the mailing over simplified funding issues in the NHS. The claims were thus misleading and could not be substantiated. Breaches of Clauses 7.2 and 7.3 were ruled.

The Panel did not consider that the mailing was such as to offend recipients or to bring discredit upon either Ferring as a company or the pharmaceutical industry as a whole and ruled no breach of Clauses 2 and 9.1 of the Code.

Complaint received **9 November 1999**

Case completed **10 January 2000**

CASE AUTH/953/11/99

SMITHKLINE BEECHAM v PASTEUR MÉRIEUX MSD

Travel vaccines journal outsert

SmithKline Beecham complained about a four page travel vaccines journal outsert produced by Pasteur Mérieux MSD. The outsert, which related to hepatitis A and typhoid vaccines, was entitled 'Relax' and one of the claims made was 'Unmatched service and support from Pasteur Mérieux MSD'. SmithKline Beecham alleged that this claim was exaggerated. It was not supportable as SmithKline Beecham had a service which was at least as good.

The Panel considered that the claim implied that, with regard to the supply of travel vaccines, the services and support offered by Pasteur Mérieux MSD were better than that offered by any other company. SmithKline Beecham had provided details of its services and support and Pasteur Mérieux MSD had provided a few examples from the range of services and support that it offered. The Panel noted that Pasteur Mérieux MSD's services and support were well received by its customers but it had not submitted any data to indicate that other companies' services and support were not equally well received. In the Panel's view the objective measurement and comparison of services and support was difficult, given that elements of service and support might differ between companies. The Panel considered that the claim was exaggerated and a breach of the Code was ruled.

SmithKline Beecham Pharmaceuticals complained about a four page travel vaccines journal outsert (ref TRO/2040/0899/M) produced by Pasteur Mérieux MSD Ltd. The outsert, designed to be stapled down the spine of a journal, was entitled 'Relax' and detailed the flexible protection afforded by hepatitis A and typhoid vaccines. Page 2 of the outsert bore three bullet points; the first two referred to vaccines while the third was 'Unmatched service and support from Pasteur Mérieux MSD'. Pages three and four bore the 'Travel Vaccines/Pasteur Mérieux MSD' logo and the strapline 'Opening up a safer world'. The outsert had been attached to GP News (24 September and 22 October) and Doctor (4 November).

COMPLAINT

SmithKline Beecham alleged that the claim 'Unmatched service and support' was exaggerated in breach of Clause 7.8 of the Code as it clearly related to the hepatitis A and typhoid vaccines to which the outsert referred. SmithKline Beecham considered that the claim was not supportable as it had a service which was at least as good. SmithKline Beecham included details of its service.

RESPONSE

Pasteur Mérieux MSD stated that the claim in question referred to the range of services and support that the company provided to all of its customers. It was not a claim for a product but a claim for the company as a whole. As this claim did not constitute a claim of a medical or scientific nature and nor was it information or a claim related to pricing and market share it was unclear why this complaint had been submitted to the Authority.

Pasteur Mérieux MSD stated that in order for another company to provide a matched service it would need to demonstrate that it matched all the services and support that Pasteur Mérieux MSD provided. This was not the case. Pasteur Mérieux MSD submitted that to list all of its services in detail would provide its competitors with commercially sensitive information. The company therefore provided a few specific examples of the range of services and support which it provided and which were unmatched by any other company.

Pasteur Mérieux MSD stated that the high regard that its customers had for its services and support was highlighted by recent market research. In a customer tracking survey general practitioners, practice managers, practice nurses and others were asked to rate a number of aspects of customer service. These were measured on a five point scale ranging from excellent to very poor. For delivery services, ranges of

vaccines, information provided, relationship with sales representatives, invoicing and administration, ordering process and vaccine availability over 70% of respondents rated Pasteur Mérieux MSD's service as excellent or good. In addition, in a recent survey of drug information pharmacists the level of service and knowledge/competence of Pasteur Mérieux MSD were both rated as excellent on a four point scale from excellent to very poor.

In summary Pasteur Mérieux MSD was concerned that the complaint was not in fact covered by the Code. If however its claim was deemed to be covered by the Code then the company trusted that it had clearly demonstrated, without compromising its commercial advantage, that its services and support were unmatched.

PANEL RULING

The Panel noted that the purpose of the outsert, and thus all of the claims therein, was to promote Pasteur Mérieux MSD's travel vaccines; it was not a corporate outsert. The outsert was therefore subject to the Code. The supplementary information to Clause 7 stated that the application of that clause was not limited to information or claims of a medical or scientific nature. It included, but was not limited to, information or claims relating to pricing and market share.

The Panel considered that the claim in question 'Unmatched service and support' implied that, with regard to the supply of travel vaccines, the services and support offered by Pasteur Mérieux MSD were better than that offered by any other company. SmithKline Beecham had provided details of its services and support and Pasteur Mérieux MSD had provided a few examples from the range of services and support that it offered. The Panel noted that Pasteur Mérieux MSD's services and support were well received by its customers but it had not submitted any data to indicate that other companies' services and support were not equally well received. In the Panel's view the objective measurement of services and support was difficult as was a direct comparison, given that elements of service and support might differ between companies. The Panel considered that the claim was exaggerated. A breach of Clause 7.8 was ruled.

During its consideration of this case the Panel noted that the mailing promoted Pasteur Mérieux MSD's hepatitis A and typhoid vaccines. Prescribing information should have been included. The Panel requested that Pasteur Mérieux MSD be advised of its views.

Complaint received **10 November 1999**

Case completed **18 January 2000**

ANONYMOUS v PROCTER & GAMBLE

Sponsorship of regional advisory board members to attend scientific meetings

An anonymous complaint was received about the sponsorship of members who sat on regional advisory boards established by Procter & Gamble. The complainant alleged that only members of the advisory boards were invited to be guests of the company at national and international scientific meetings and that this was a unique policy at variance with practice elsewhere in the pharmaceutical industry.

The complainant alleged that each year the company would indicate which meetings it would be supporting and regional advisory board members would be able to attend one meeting for which they would be paid a travel grant of £3,500. The complainant stated that it was unclear what mechanism the company had put in place to recoup the balance of the travel grant if the cost of the travel arrangements was less than £3,500.

The Panel noted that the company did not pay a consulting fee to advisory board members, although the chairmen received a modest honorarium. The Panel noted that whilst the Code did not stipulate requirements regarding the selection by companies of delegates to sponsor to attend meetings, the overall arrangements had to comply with the Code. It was not necessarily a breach of the Code to sponsor solely health professionals who sat on the company's regional advisory boards.

The Panel noted that each advisory board member was not paid a travel grant of £3,500 as alleged. The amount available depended on the location of the meeting and the cost of travelling. For air fares the upper limit was set at the cost of a business class ticket which did not appear to the Panel to be unreasonable. £3,500 had been set as the upper limit for travel to a specific meeting in America. Only legitimate expenses were reimbursed and receipts were required. The Panel did not consider that the arrangements and the sponsorship were inappropriate as alleged. No breach of the Code was ruled.

An anonymous complaint was received about the activities of Procter & Gamble Pharmaceuticals UK, Limited.

COMPLAINT

The complainant stated that Procter & Gamble had been operating a network of regional advisory boards in the field of osteoporosis throughout the UK for a number of years. These boards were originally provided by Procter & Gamble as a means for clinicians involved in osteoporosis services (and those who hoped one day to run such services) to meet and share information in a rapidly developing area of medicine in the early 1990s. Each board had a chairperson and there was a further national board attended by these chairpersons. Boards were encouraged to develop newsletters dealing with topics of relevance in osteoporosis and these newsletters were circulated in each locality to general practitioners amongst others. Membership of a board involved signing a confidentiality clause on a regular basis, presumably cementing and formalising the relationship between the individual doctor and the company.

The complainant explained that initially the chairpersons were invited to attend international scientific meetings as guests of Procter & Gamble. With the passage of time, individual members of the various regional advisory boards were also invited to attend scientific meetings (national and international) under arrangements which were presumably similar to those enjoyed by the chairpersons. It seemed that only members of these advisory boards were invited to be guests of Procter & Gamble at any scientific meetings to which UK doctors were invited. This would appear to be a policy unique to this company and at variance with practice elsewhere within the pharmaceutical industry.

The complainant stated that no one would object to reputable pharmaceutical companies providing appropriate support to enable doctors to attend *bona fide* scientific meetings especially when these were held outside the UK. Traditionally, travel and conference fees for meetings held outside the UK were high and reimbursement of such expenses legitimately incurred had not been a priority for the NHS. Were it not for the support of the pharmaceutical industry, much of this valuable postgraduate activity would be unavailable to doctors working in the NHS.

The complainant stated that Procter & Gamble had recently changed its travel arrangements for doctors from the UK (who would presumably still be members of one of the regional advisory boards) who attended an international scientific meeting to which the company was inviting guests. Each year the company would indicate which meetings it would be supporting and regional advisory board members would be able to attend one meeting for which they would be paid a travel grant of £3,500. Each individual doctor would be expected to make his or her own travel arrangements and the company would continue to pay directly on behalf of the doctors attending the meeting the appropriate conference and hotel fees for the duration of the conference. The complainant stated that it was unclear (i) what mechanism the company had put in place to recoup the balance of the travel grant if the cost of the travel arrangements was less than £3,500 and (ii) the mechanism put in place by the company to enable doctors to submit receipts for the travel arrangements they made with the travel grant. This seemed an unorthodox means of arranging travel to scientific meetings which of themselves of course continued to be perfectly reputable. Once again, this approach was to the complainant's knowledge unique to Procter & Gamble and this could, however unintentionally, appear to blur the normally clear distinction between a 'payment' and 'reimbursement of legitimate travel

expenses' (which would be supported with appropriate receipts).

RESPONSE

Procter & Gamble stated that it tried to be scrupulous in the care it took in relation to sponsorship of health professionals to attend scientific meetings. It was aware that this had been a topical area and it had put in place policies that were consistent with the letter and spirit of Clause 19.1 of the Code.

Procter & Gamble's sponsorship of health professionals to scientific meetings

It was true that Procter & Gamble established some years ago groups of advisers that administratively were organised as regional advisory boards (RABs). In the same way as many other companies had done, it had developed a RAB programme in the fields of most interest to the company given its own research and development focus. The treatment of osteoporosis was a major therapeutic area of interest and RABs were established to encourage physicians to work together to increase local awareness, diagnosis, and management of osteoporosis. In addition, they had the ancillary benefit of serving as a resource for providing expert advice to the company. As the complainant noted, in the 1990s this had been an important and rapidly developing area of medicine. Procter & Gamble believed that it had made material contributions in this field.

Reflecting the areas which were relevant to improving Procter & Gamble's understanding of osteoporosis and its management, the RABs had individuals representing multiple disciplines (eg rheumatology, endocrinology, geriatrics, etc) and differing expertise in treatment options (hormone replacement therapy, selective oestrogen receptor modulators, calcium/vitamin D, bisphosphonates etc). The focus of the RAB members was, therefore, very wide and, whilst the boards benefited Procter & Gamble by, from time to time, allowing an interchange of ideas and the provision of advice relevant to its specific products, the boards' activities were not focused on any particular product but on improving understanding of the therapeutic field as a whole.

RAB members were recruited on the basis of their interest in osteoporosis generally within their region/locality and the recommendation for new participants frequently came from existing RAB members. Administratively, as it covered the whole country, there were 10 RABs with approximately 8-10 members on each. Because from time to time Procter & Gamble disclosed proprietary and confidential information to such members in connection with seeking expert advice, members agreed to keep confidential any technical and business information or data that was not in the public domain. It was entirely wrong to suggest, as the complainant did, that the whole relationship was shrouded in confidentially through clauses signed 'on a regular basis'. In fact, the agreements were signed for one year and Procter & Gamble went so far as to state expressly that any information provided to members could be freely disclosed and used without limitation, unless this was identified as proprietary and confidential information. In the normal way, it said that the confidentiality obligation ceased when the information became available to the public other than as a result of a breach of a member's obligations.

Procter & Gamble stated that it was important to note in the context of sponsorship to attend scientific meetings that the company did not pay any consulting fee in respect of membership of a RAB except to the chairman, who received a modest honorarium for the administrative time that he/she spent. For other members, the recompense was Procter & Gamble's willingness to sponsor the health professional to attend one international and one local meeting per year in the relevant field (if they choose to do so) and the projects that the RAB members themselves were able, through the faculty of the boards, to mobilise in the area of osteoporosis (independently of Procter & Gamble financially).

Meeting selection and invitees

Procter & Gamble stated that there was nothing unusual about the selection process given that the scientific meetings in question were relevant to osteoporosis. The sponsorship arose out of the advisory board consultancies and whilst Procter & Gamble had sponsored attendance at various high quality scientific meetings, the attendance it most often sponsored was either to the National Osteoporosis Society meeting in the UK or the American Society for Bone and Mineral Research (ASBMR). The meeting selection might change based on the scheduling of conferences or soundings as to the current interests of board members but the basic approach was to sponsor attendance at one international and one national meeting per year. At some of these meetings, Procter & Gamble also organised satellite symposia and it obviously encouraged persons it sponsored to attend these meetings if they were able to do so.

The fact that the offer was made to members of the RABs who had already shown a real commitment to medical and scientific developments in the relevant field ensured administrative efficiency and increased the prospects of the sponsorship being properly utilised. As Procter & Gamble provided no financial benefit to RAB members beyond supporting attendance at scientific meetings with very clear educational content, it knew that members must really value the attendance support it provided.

Number of health professionals involved

Procter & Gamble stated that there were up to 89 RAB members country-wide and each was offered sponsorship. Inevitably, the ability of members to take up an offer of attendance sponsorship depended upon a host of factors including availability at the time of the meeting and the specific programme. Suffice it to say, historically it had found that less than half of the invitations were liable to be accepted; just over 40 was quite normal, although on occasions the acceptance rate had been as low as 10 or as high as 60, depending on the content of the meetings.

Arrangements for the payment of travel grants

Procter & Gamble stated that the complainant had a totally distorted picture of the arrangements the company made for payment of travel expenses. Procter & Gamble needed to give some indication to board members of the amount it was prepared to provide to support attendance at meetings. For each meeting, Procter & Gamble worked with a travel agency to identify the going rate for travel. Air fares varied according to where the board member was based, but the travel agency indicated, for instance, that the value of a business class ticket from London to St Louis (this year's venue for the ASBMR meeting) was about £3,500. This was then established as the budget limit. For last year's European meeting (European Calcified Tissue Society) which was held in Maastricht, the value was £450. The complainant appeared to have picked up the figure of £3,500 for the recent St Louis conference and assumed that it guaranteed such a payment for all meetings. This was quite wrong. All were budget limits only and directions were given to retain receipts for reimbursement of actual expenses. It only reimbursed for legitimate expenses properly incurred and did not reimburse above the value of those expenses. This was demonstrated by the standard documentation for the invitation to the St Louis meeting that appeared to have precipitated the complaint, a copy of which was provided.

Procter & Gamble stated that beyond that, no spouses were invited or paid for and hospitality met the requirement of being secondary to the meeting and proportionate (usually an invitation to a conference dinner).

Conclusion

Procter & Gamble noted that the complainant was not raising any objection to the company providing appropriate support to enable health professionals to attend proper scientific meetings, especially when these were held outside the UK. He/she accepted that even specialists had limited support from the NHS for attendance. The company agreed with the complainant that were it not for sponsorship by the pharmaceutical industry, attendance at major scientific conferences would be out of reach for many doctors. Procter & Gamble stated that its sponsorship enabled physicians to stay up-to-date with the latest scientific information in the field. Contrary to the suggestions made, however, the arrangements were not only designed to encourage attendance by persons motivated to use the occasion in a professionally productive way but also involved administrative procedures entirely within the Code.

PANEL RULING

The Panel noted that Clause 19.1 stated that companies were permitted to provide appropriate hospitality to members of the health professions and appropriate administrative staff in association with scientific and promotional meetings, scientific congresses and other such meetings. The supplementary information to Clause 19.1 stated that the provision of hospitality included the payment of reasonable, actual travel costs which a company might provide to sponsor a delegate to attend a meeting.

The Panel noted that the regional advisory boards were established to increase local awareness, diagnosis and management of osteoporosis as well as occasionally providing advice and exchanging ideas with the company. The Panel noted that the company did not pay a consulting fee to advisory board members, although each chairman received a modest honorarium. The company was willing to sponsor members to attend one local and one international meeting per year relevant to osteoporosis. Historically less than half the invitations tendered were accepted. The arrangements might be seen as a payment to advisory board members. The Panel noted that whilst the Code did not stipulate requirements regarding the selection by companies of delegates to sponsor to attend meetings the overall arrangements had to comply with the Code. It was not necessarily a breach of the Code to sponsor solely health professionals who sat on the company's regional advisory boards. It might be unacceptable to pay a consultancy fee to the members of the advisory board as had been decided in a previous case (Case AUTH/686/3/98). The overall arrangements needed to comply with Clause 19.1 of the Code.

The Panel noted that each advisory board member would not be paid a travel grant of £3,500 as alleged. The amount available depended on the location of the meeting and the cost of travelling to the venue. For air fares the limit was set at the cost of a business class ticket. Only legitimate expenses were reimbursed and receipts were required.

The Panel noted that the proforma letter inviting recipients to a symposium at the 21st Annual Meeting of the American Society for Bone and Mineral Research referred to reimbursement for return flights to St Louis to a maximum value of £3,500 and stated that 'Costs incurred will be refunded upon receipt of an invoice together with receipts'. Proforma invoices for air fare and travelling expenses each referred to reimbursement of travel costs and required the production of receipts.

The Panel noted that delegates were merely reimbursed for legitimate expenditure incurred. To set an upper limit on the expenditure to be incurred in respect of air fares did not appear to the Panel to be unreasonable. The Panel did not consider the arrangements and the sponsorship were inappropriate as alleged. No breach of Clause 19.1 of the Code was ruled.

Complaint received **11 November 1999**

Case completed **6 December 1999**

CODE OF PRACTICE REVIEW – FEBRUARY 2000

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

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949/10/99	**Social Audit v Pharmacia & Upjohn**	**Detrusitol journal advertisement**	**Breach Clause 7.2**	**No appeal**	**Page 98**
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953/11/99	**SmithKline Beecham v Pasteur Mérieux MSD**	**Travel vaccines journal outsert**	**Breach Clause 7.8**	**No appeal**	**Page 113**
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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, more than 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 such medicines made available to the general 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 or buy medicines by the gift, offer or promise of any benefit or bonus, whether in money or in kind
- the provision of hospitality
- the organisation of promotional meetings
- the sponsorship of scientific and other meetings including payment of travelling and accommodation expenses in connection therewith
- the provision of information to the general public either directly or indirectly
- 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.

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 Philip Cox 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 should be sent to the Director of the Prescription Medicines Code of Practice Authority, 12 Whitehall, London SW1A 2DY (telephone 0171-930 9677 facsimile 0171-930 4554).