PRESCRIPTION MEDICINES
CODE OF PRACTICE AUTHORITY

CODE OF PRACTICE REVIEW

NUMBER 12 MAY 1996

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.

Naming names in case reports

Significant changes to case reports apply in relation to complaints received from this year onwards.

Comprehensive and detailed reports of the outcomes of complaints made under the Code of Practice have now been published for about ten years. Reports have named the company against which the complaint had been made and the name of the medicine involved, but only if a breach of the Code had been ruled. Where no breach had been ruled, the identity of the company and of the product have been kept confidential, often resulting in reports which were uninformative and obscure and thus of little educational value.

Thanks to changes agreed by member companies of the ABPI at its Half-Yearly General Meeting last year, reports on complaints received on and after 1 January 1996 will all name the company and the medicine involved regardless of whether or not a breach of the Code has been ruled.

The Authority welcomes this move to total transparency which it believes will be in the industry's interest and will avoid the perception that the reason for confidentiality in no breach cases was because there was something to hide - which was not the case.

It is already the practice to name all companies making complaints, whether or not a breach of the Code is ruled and this will continue. Organisations making complaints will be named but the information provided will not be such as to identify any particular individual. The names of health professionals and others making complaints will remain confidential.

This issue of the Review contains some reports of complaints where no breach was ruled and where the identity of the respondent company remains undisclosed because the complaint was received prior to 1 January 1996. Other reports, which relate to complaints received after 1 January, reveal the name of the company involved even where no breach was ruled.

All complaints received before 1 January have now been reported and this is therefore the last issue of the Review which will include anonymous reports.

Examinations for representatives.

Clause 16.2 of the Code states that representatives must pass the appropriate ABPI representatives examination within two years of starting such employment.

The supplementary information to Clause 16.2 makes it clear that representatives must pass the appropriate examination within two years irrespective of whether those two years are spent with one company or with more than one company. A representative cannot, for example, do eighteen months with one company and eighteen months with another and so on and thus avoid the examination entirely.

These points are drawn to the attention of companies because the ABPI has informed us that candidates are on occasion entered for the examination who have already been employed as a representative for more than two years.

Companies are advised to ensure that when commencing employment new representatives are made fully aware of the examination requirements which apply to them.

Extenuating circumstances

The supplementary information to Clause 16.2 states that in extenuating circumstances, such as prolonged illness, the Director of the Prescription Medicines Code of Practice Authority may agree to the continued employment of a person as a representative past the end of the two year period, subject to the representative passing the examination within a reasonable time.

Pregnancy will be regarded as such an "extenuating circumstance" and the two years extended upon application when the person concerned returns to employment as a representative at the end of statutory maternity leave.

Chief executives must authorise inter-company complaints.

Companies are reminded that Paragraph 5.2 of the Constitution and Procedure for the Prescription Medicines Code of Practice Authority states that, when a complaint is made by a pharmaceutical company, the complaint must be signed or authorised in writing by the company's chief executive and must state the clauses of the Code which are alleged to have been breached.

Time is often wasted because these requirements are not complied with and companies are asked to bear them in mind.

Advance notification of new products or product changes

Advice on the provision of information on new products in advance of them receiving a marketing authorization to health authorities and trust hospitals etc for estimation of likely budgets was first given by the ABPI in 1992 and was incorporated, in a slightly modified form, in the supplementary information to Clause 3.1 in the 1996 edition of the Code of Practice.

Only three complaints touching upon this advice have been made since it was first given (two of them concerning the same material) and the outcomes of these are reported in this issue of the Review (Case AUTH/336/9/95 with Case AUTH/320/11/95, which went to appeal, and Case AUTH/371/11/95). Two of the complaints came from the Medicines Control Agency. A breach of Clause 3.1 was ruled in each case and it may accordingly be helpful to reiterate and enlarge upon the advice already available.

The supplementary information to Clause 3.1 provides that;

i) the information must relate to:
   (a) a product which contains a new active substance, or
   (b) a product which contains a newly synthesized active substance, or
   (c) a product which is to have a significant addition to the existing range of authorized indications, or
   (d) a product which has a novel and innovative means of administration

ii) there must be significant budgetary implications

iii) only factual information must be provided, including an indication of the likely cost, and it must not be presented in the style of promotional material

iv) information should not be directed to those who would be expected to prescribe the product, but to those concerned with budgets

v) if requested, further information may be supplied or a presentation made.

The following additional points were established during the consideration of the recent complaints and have the approval of the Code of Practice Appeal Board. To be acceptable:

a) the budgetary implications must be indicated and must be such that they will make significant differences to the likely expenditure of health authorities and trust hospitals and the like

b) the information should be limited to that sufficient to provide an adequate but succinct account of the product's properties

c) the information should primarily be about the product itself - critical comparisons of other products must be avoided and existing products mentioned only to put the new product into context in the therapeutic area concerned

d) the information may be attractively presented and printed but should not be in the style of promotional material - product specific logos should be avoided but company logos may be used

e) the brand name of the product may be included in moderation in the material but it should not be stylised or put in capitals or used to excess

f) the information provided should not include mock up drafts of either summaries of product characteristics or patient information leaflets.

How to contact the Authority

Our address is:

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

Telephone: 0171-930 9677
Facsimile: 0171-930 4554

Copies of the Code of Practice for the Pharmaceutical Industry and of this Review can be obtained from:

Emer O'Reilly on
0171-930 9677 extn 1443.

Direct lines can be used for the members of the Authority.

David Massam 0171-747 1405
Heather Simmonds 0171-839 1058
Jane Landles 0171-747 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.

The Internet and the Code of Practice for the Pharmaceutical Industry

The Code of Practice Appeal Board has suggested that the following article on the Internet and the Code written by Heather Simmonds, the Authority's Secretary, which has been published elsewhere, should be reprinted in the Review.

BACKGROUND

History & Operation of the Code

The Association of the British Pharmaceutical Industry (ABPI) has a code of practice, the Code of Practice for the Pharmaceutical Industry[1] which was established in 1958 by the ABPI to control the promotion of medicines to members of the health professions. It has been regularly updated since and the current edition came into operation on 1 January 1996.

The Code applies to the promotion of medicines to members of the health professions and to appropriate administrative staff such as, for

example, hospital managers. It covers journal and direct mail advertising, the activities of representatives, including material used by representatives, the supply of samples, the provision of inducements, the provision of hospitality, the sponsorship of meetings, the provision of information to the general public and all other sales promotion in whatever form. When the Code was originally agreed in 1958 it was very much with printed promotional material in mind. Such modern developments as e-mail and the Internet were not even dreamt of at that time. The Code is amended on a regular basis and a recent change takes account of the use of e-mail. The principles of the Code apply whatever the mechanism of communication.

The Prescription Medicines Code of Practice Authority was established by the ABPI in 1993 to operate the Code of Practice for the Pharmaceutical Industry independently of the ABPI itself. The Constitution and Procedure for the Code of Practice Authority appears at the back of the Code of Practice booklet.

Compliance with the Code is obligatory for ABPI member companies and in addition some 50 non member companies have voluntarily agreed to comply with the Code and to accept the jurisdiction of the Authority.

Complaints Procedure

Complaints submitted under the Code, the majority of which are from healthcare professionals, 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 expert advice where appropriate. The Code of Practice Panel makes a decision in every case. If the Panel rules no breach of the Code this can be appealed by the complainant and if the Panel rules a breach of the Code this can be appealed by the respondent. Appeals are heard by the Code of Practice Appeal Board which is chaired by an independent, legally qualified chairman and includes three medically qualified independent members, an independent pharmacist, and an independent member from a body which provides information on medicines. The remainder of the Appeal Board is made up of eight senior executives and four medical directors of pharmaceutical companies. The Appeal Board is the final arbiter on complaints under the Code of Practice.

Where a breach of the Code is ruled the company concerned must give an undertaking that use of the material and/or the practice in question has ceased forthwith and that all possible steps have been taken to avoid a similar breach of the Code 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. Reports on all cases are published by the Authority in the Code of Practice Review[2].

Legal Requirements in the UK

In addition to the Code there are a number of legal requirements in the UK relating to the promotion of medicines. The Medicines Act 1968[3] includes some requirements relevant to advertising. The regulations that are the most important are The Medicines (Advertising) Regulations 1994[4]. These Regulations set out the requirements for promotion of medicines to both the public and the health professionals. The Code reflects and extends beyond the legal requirements. The relevant legal requirements are listed in the back of the Code of Practice booklet.

The 1994 Regulations implement in the UK the EC Council Directive on the advertising of medicinal products for human use[5]. Harmonisation in this area in EC states is far from complete as certain requirements were left to individual member states to determine. For example, the number of samples that can be provided to a health professional is limited to one per product per year in Finland and Norway, ten in the UK and, in Belgium, a total of no more than 600 samples per year for all products.

Scope of the ABPI Code

The scope of the Code is given in Clause 1 which states that the Code applies to the promotion of medicines to members of the UK health professions and to appropriate administrative staff and to information to be made available to the general public about medicines so promoted.

The ABPI Code does not apply to the promotion of over-the-counter medicines to members of the health professions when the object of that promotion is to encourage their purchase by members of the general public. These advertisements are covered by the Proprietary Association of Great Britain (PAGB) Code of Practice for Advertising Over-the-Counter Medicines to Health Professionals and the Retail Trade[6]. The ABPI Code does not apply to advertisements for over-the-counter medicines to the general public for self medication purposes. These advertisements are covered by the PAGB Code of Standards of Advertising Practice for Over-the-Counter Medicines[7].

The definition of promotion given in Clause 1.2 of the Code is any activity undertaken by a pharmaceutical company or with its authority which promotes the prescription, supply, sale or administration of its medicines.

Application of the Code

It is sometimes difficult to determine whether or not particular material comes within the scope of the Code of Practice. The lack of reference to a product name does not necessarily mean that the material is outside the Code. For example, it has been established that company produced material on a disease area in which the company has a commercial interest does come within the scope of the Code even if no product name is mentioned or implied. In the case in which this question arose it was considered that the material was clearly produced as part of the general promotional background for specific products. Another example relates to advertisements in international journals. The supplementary information to Clause 1.1 of the Code states that advertisements in international journals which are produced in English in the UK are subject to the Code even if only a small proportion of the circulation is to a UK audience.

THE SCOPE OF THE CODE AND THE INTERNET

The Internet is not mentioned in the Code. Nor is it mentioned in any of the legal requirements. The Authority has not received any complaints to date about information available on the Internet although it has received numerous enquiries. The Authority can only give an informal view on any matter as it is not the final arbiter; that is the role of the Code of Practice Appeal Board. If a complaint were received about the Internet, the Code of Practice Panel's rulings could be overturned by the Code of Practice Appeal Board upon appeal. It should be borne in mind that the views expressed in this guidance are informal, for discussion purposes, and are intended to raise awareness of the appropriate clauses of the Code that need to be considered. Complaints received about material on the Internet would be taken up with the appropriate company in the UK in the first instance as the Code only applies to companies in the UK. A UK

company has been ruled in breach of the Code in relation to an advertisement which the parent company (operating outside the UK) placed in a UK publication.

Following on from established precedent concerning advertising in international journals etc, the Code would apply to information put on the Internet by companies operating in the UK as the information would be accessible to a UK audience. Companies in the UK should not put information on the Internet in countries outside the UK in an attempt to avoid the requirements of the UK Code.

Turning now to companies outside the UK, the Authority's view is that if the information was put on the Internet in a country outside the UK and it referred specifically to the UK use of a product, then the UK Code would apply. For example, if a company in the US put information on the Internet relating to both the US use of a product and to the UK use of the product, the information about the UK use of the product would be subject to the UK Code. The information about the US use of the product would not come within the scope of the UK Code. If a company in the US put general information about a product on the Internet in the US it would not come within the scope of the UK Code provided the information did not refer specifically to the UK use of the product. Obviously if the product was only available in the UK, the information would have to comply with the UK Code.

The requirements of the Code which apply depend to a certain extent on the accessibility of the information on the Internet. This can be divided into two. Firstly, that open to all, and, secondly, that for access only by health professionals and appropriate administrative staff.

ACCESS OPEN TO ALL

In this situation the material will be accessible to the general public and the requirements of Clause 20 which deals with relations with the general public and the media would be relevant. Under Clause 20.1 it is a breach of the Code (and it is also a breach of the 1994 advertising regulations) to advertise a prescription only medicine (POM) to the general public. This restriction also applies to medicines which are not POM but cannot be legally advertised to the general public. For example, insulin is legally classified as a pharmacy medicine (P) and it is therefore available from a pharmacy without a prescription but it cannot be advertised to the general public due to a prohibition in the 1994 advertising regulations. It thus follows that pharmaceutical companies cannot put advertisements for certain products on the Internet. Advertisements on the Internet for over-the-counter medicines which are intended to induce their purchase rather than their prescription are not covered by the ABPI Code and companies would need to contact the PAGB for further information. The PAGB preapproves all advertising of medicines to the general public.

Clause 20.2 permits companies to make available information about medicines to the general public provided it meets certain criteria. The information must be factual and be presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. Statements must not be made for the purpose of encouraging members of the public to ask their doctors to prescribe a specific medicine.

The supplementary information to Clause 20.2 permits companies to provide summaries of product characteristics (SPCs) or data sheets to members of the public on request. These documents are approved by the Medicines Control Agency (MCA). Companies can also provide copies of patient pack information leaflets to the public on request. Data sheets and some patient pack information leaflets are already available to the public as they are published in either the ABPI Data Sheet Compendium[8] or the ABPI Patient Information Leaflet Compendium[9] which can be found in reference libraries or purchased directly from Datapharm Publications Limited. It would be acceptable for companies to put the approved SPC, or data sheet, and the patient pack information leaflet on the Internet. Companies must not edit the material to, for example, highlight certain information or draw attention to particular sections. The material must be faithfully reproduced on the Internet. Edited versions could be seen as being advertisements for the products to the general public which is prohibited in the case of certain medicines (all POMs and some P medicines). The supplementary information to Clause 20.2 allows for the provision of financial information made available to inform shareholders, the Stock Exchange and the like by way of annual reports and announcements etc. Such information may relate to both existing medicines and those not yet marketed and can be put on the Internet provided it is factual and presented in a balanced way.

Clause 20.3 requires that requests from individual members of the public for information or advice on personal medical matters must be refused and the enquirer recommended to consult his or her own doctor. This would apply to requests sent by e-mail.

Companies could respond to requests for information using e-mail provided the response was in accordance with the Code.

Companies do produce very useful information for the general public on disease areas etc which complies with Clause 20 and there is no reason why this could not be included on the Internet. The supplementary information to Clause 20.2 states that information on medicines made available under Clause 20.2 should be examined by pharmaceutical companies to ensure that it does not contravene the Code or relevant statutory requirements.

The other clauses that might be appropriate in these circumstances are Clauses 2, 9.1 and 9.9. Clause 2 states that methods of promotion must never be such as to bring discredit upon or reduce confidence in the pharmaceutical industry and Clause 9.1 requires that material must not be likely to cause offence and that high standards must be maintained at all times. Clause 9.9 of the Code requires that all material relating to medicines and their uses which is sponsored by a pharmaceutical company must clearly indicate that it has been sponsored by that company.

RESTRICTED ACCESS

Where access to information is restricted to healthcare professionals and appropriate administrative staff only by way of a secure closed system, then pharmaceutical companies could put promotional material on the Internet provided that it met all the relevant requirements of the Code. In such circumstances the material would be no different to printed promotional material. Prescribing information in accordance with Clause 4.2 of the Code would need to be provided. If the material is more than one "screen" in length, then the instructions for accessing the prescribing information or a statement that the prescribing information appears at the end of the material, should be give on the first "screen" in accordance with the principles of Clause 4.3. It would not be

sufficient to refer to the SPC or data sheet for two reasons. Firstly, the cost must be given in prescribing information and this is not included in the SPC or data sheet. Further, the prescribing information is in certain respects only a summary of the SPC or data sheet. Secondly, each promotional item must stand alone in relation to the Code.

The general principles of the Code are probably best summed up by Clause 7.2 which requires that information, claims and comparisons must be accurate, balanced, fair, objective and unambiguous and must be based on an up-to-date evaluation of all the evidence and reflect that evidence clearly. They must not mislead either directly or by implication. Clause 7.3 requires that any information, claim or comparison must be capable of substantiation. Substantiation must be provided without delay to members of the health professions or appropriate administrative staff on request. Clause 3 prohibits a company from advertising prior to the grant of the marketing authorization and requires that material must be in accordance with the marketing authorization and not inconsistent with the SPC or data sheet. Clause 9.1 requires 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 Code also requires in Clause 9.8 that the telephone, telemessages, telex, facsimile machine and e-mail must not be used for promotional purposes except with the prior permission of the recipient. If companies wish to e-mail doctors with promotional material they must obtain permission prior to commencing such activities. The requirements of this clause originate in the view that healthcare professionals would be annoyed if their means of communication were continually blocked by pharmaceutical companies using them for promotional purposes.

Clause 9.9 requires that all material sponsored by a pharmaceutical company must clearly indicate that it has been sponsored by that company and would apply to sponsorship of items on the Internet. If a company were to sponsor a facility on the Internet whereby health professionals could communicate about various diseases and products etc, then companies would need to be careful to ensure that the information contributed complied with the Code. It would be unacceptable, for example, if a doctor placed information on the Internet relating to the unlicensed use of a product via a facility sponsored by a pharmaceutical company. This could be seen as the company promoting the product outside its licence as the company would in effect be distributing the information. An example of this principle in relation to printed promotional material would be if a doctor published a letter in a medical journal concerning the use of a product in an unlicensed indication. Doctors are not prohibited from prescribing medicines for unlicensed indications. If, however, the pharmaceutical company that marketed the product decided to buy reprints of the published letter and distribute them to general practitioners this would be seen as promotion of that medicine for an unlicensed indication in breach of Clause 3.2 of the Code.

A pharmaceutical company that places material on the Internet will of course need to certify hard copies of the material in accordance with the requirements of Clause 14 of the Code whereby promotional material must not be issued unless its final form has been certified by two persons on behalf of the company, one of whom must be a doctor and the other an appropriately qualified person. The certificate must certify that the signatories have examined the final proof of the material and that in their belief it is in accordance to the requirements of relevant advertising regulations and the Code and is not inconsistent with the marketing authorization and the SPC or data sheet and is a fair and truthful presentation of the facts about the medicine. Material which is still in use must be recertified at intervals of no more than two years. Companies are required to preserve all certificates together with the material in the form certified and information indicating the person to whom it is addressed, the method of dissemination and the date of first dissemination.

CONCLUSIONS

The use of the Internet by pharmaceutical companies raises a number of difficult issues some of which have been discussed above. It should be borne in mind that the views expressed above are informal and are intended for discussion purposes and to raise awareness of the appropriate clauses of the Code that need to be considered. At its simplest the Internet is merely another means of communication with the principles of the Code applying equally to information on the Internet.

It is acknowledged that the internationalism of the Internet causes problems with jurisdiction and will continue to do so. Complaints about information on the Internet will have to be judged on their own particular circumstances. In time case precedents will clarify the issues and provide further guidance.

References

1 ABPI Code of Practice for the Pharmaceutical Industry 1996 edition. Available from the Prescription Medicines Code of Practice Authority, (PMCPA)
12 Whitehall, London SW1A 2DY
telephone 0171 930 9677
facsimile 0171 930 4554

2 Code of Practice Review
Issued on a quarterly basis and available from the PMCPA

3 The Medicines Act 1968 Part VI Promotion of Sales of Medicinal Products.

4 The Medicines (Advertising) Regulations 1994 No.1932.

5 Council Directive 92/28/EEC of 31 March 1992 on the advertising of medicinal products for human use.

6 Code of Practice for Advertising Over-the Counter Medicines to Health Professionals and the Retail Trade. Available from the Proprietary Association of Great Britain (PAGB) Vernon House, Sicilian Avenue, London WC1A 2QH, telephone 0171 242 8331.

7 Code of Standards of Advertising Practice for Over-the-Counter Medicines.
Available from the PAGB as above.

8 ABPI Data Sheet Compendium.
Available from Datapharm Publications Limited,
12 Whitehall, London SW1A 2DY
telephone 0171 930 3477
facsimile 0171 747 1411.

9 ABPI Patient Information Leaflet Compendium. Available from Datapharm Publications Limited, as above.

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 procedure 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 are:

Friday, 26 July 1996
Wednesday, 25 September 1996
Wednesday, 23 October 1996

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 Emer O'Reilly at the PMCPA for details (0171-930 9677 extn 1443)

CASE AUTH/323/8/95

ABBOTT v PFIZER

Promotion of Zithromax

Abbott complained about a number of promotional items issued by Pfizer and its division Richborough in relation to Zithromax (azithromycin). It was alleged that the choice of breakpoints employed in a featured study biased the study in favour of azithromycin, that the reader was encouraged to extrapolate *in-vitro* data to a clinical setting, that there were no clinical data to support the implied significance of these *in-vitro* data and that it had not been stated that the data were interim data.

The Panel took advice from an independent expert on the question of breakpoints as it was aware that this was a contentious area. On the advice received, the Panel ruled no breach of the Code. The Panel ruled that a Zithromax dosage card was misleading as it failed to make sufficiently clear the limitations of the data and the fact that they might not be translated into clinical results. A journal advertisement and a brochure were considered not to have breached the Code in this respect. No breach was ruled in relation to the use of interim data.

COMPLAINT

Abbott Laboratories Limited complained about a number of promotional items produced by Pfizer Limited, and its division Richborough Pharmaceuticals. The promotional materials were a Zithromax card (ref 70632 January 1995), a four page brochure headed "Antibiotic Resistance to *Haemophilus Influenzae*" (ref 70664a April 95) and a two page advertisement for Zithromax in GP, 11 April 1995 (ref 70699 July 1995) which featured interim multicentre *in-vitro* data on azithromycin, erythromycin and clarithromycin. Abbott alleged that use of the data contravened Clauses 7.1 to 7.8 inclusive and Clause 8.1 for the following reasons:

1 The selection and interpretation of breakpoints employed in the study biased the result in favour of azithromycin. This was particularly so in the case of *Haemophilus influenza* when phenotypically distinct resistant strains were rarely, if ever, seen. The erythromycin breakpoint used was to the left of the normal distribution; the clarithromycin breakpoint used was positioned over the peak whilst the azithromycin breakpoint used was placed to the right of the mode. Even if the reader requested source data, specialist knowledge was required to understand the methods of analysis used and to interpret them correctly.

2 As used, the reader was encouraged to extrapolate *in-vitro* data to a clinical scenario. The appearance of the qualifying caveat "*in-vitro* data may not directly translate into clinical results" did little to assist the reader in interpretation of the data when a) juxtaposed with a smiling human face and the words "Nationally trusted", and b) the word "effective" was used in the context of both *in-vitro* data and the clinical setting as in the claims "Zithromax - highly effective against *Haemophilus influenza (in vitro)*" and "Effective, acceptable, simply 3 days".

This misleading impression was compounded by the appearance of the claim "[ZITHROMAX]..... is the most effective [*in-vitro*] of the currently available macrolides against *H influenza*." Again, the appearance of the words "*in-vitro*" did little to prevent the reader from being misled.

3 There were no clinical data to support the implied clinical significance of these *in-vitro* data. There were clinical data which correlated well with susceptibility testing data *when analysed by currently used methods*. This compounded the misleading nature of the data when presented in isolation in promotional items.

4 The data were interim. This was not stated in any piece employing the data.

RESPONSE

Pfizer responded using the same numbers as Abbott.

1 It was stated by Abbott that the breakpoints biased the results in favour of azithromycin. Abbott supported this by noting that the erythromycin breakpoint used was to the left of the normal distribution, the clarithromycin breakpoint used was positioned over the peak while the azithromycin breakpoint used was placed to the right of the mode.

The breakpoints noted by Abbott were a reflection of the difference in activities of the agents coupled with the poor bioavailability of erythromycin. Azithromycin was approximately twice as active *in vitro* as clarithromycin (Barry et al). In Pfizer's view, the most acceptable way to determine breakpoints was to take account of the expertise of the National Committee for Clinical Laboratory Standards (NCCLS) or the British Society for Antimicrobial Chemotherapy (BSAC) Working Party. The NCCLS breakpoints (below which an organism was susceptible) for azithromycin and clarithromycin were 4mg/l and 8mg/l respectively. Breakpoints were not given by the NCCLS for erythromycin but the BSAC recommended 0.5. For these reasons, the breakpoints were chosen in the study.

2 Pfizer denied that the reader was encouraged to extrapolate the *in vitro* data to the clinical setting since it was made quite clear in the promotional items that the data were obtained *in vitro*. For example, in the journal advertisement it was made apparent on four occasions that the data were not obtained in a clinical setting. Also, it was made absolutely clear there and in the other pieces that the data were *in vitro* and that *in vitro* data may not directly translate into clinical results. Pfizer did not feel that it could be any more explicit than this.

The words "effective, acceptable and simple" had been used in promotional material since the launch of Zithromax in 1991 to describe the product as an effective antibiotic, acceptable to patients with a simple, three day course of treatment. To Pfizer's knowledge, they had not given rise to any confusion. The use of the word "effectiveness" when referring to the *in vitro* data did not

imply a direct relationship to clinical efficacy and, in Pfizer's view, it would not be so interpreted by the medical profession. The headline "Nationally trusted" was of more recent origin but, similarly, Pfizer did not consider that it would be linked by the medical reader to the data relating to resistance.

3 Since the data presented were not intended to represent efficacy in the clinical setting, no such data were provided. The method used for obtaining the susceptibility data was, as stated above, based on reputable guidelines currently used.

4 The results were indeed interim in that they applied to 320 isolates as opposed to 460 in the complete study. However, the principal investigator had indicated to Pfizer that these were very much what he expected and anticipated no significant overall change when the study was complete. Pfizer had been advised informally by the coordinator of the final data, which indeed showed no significant or overall change from the interim data. Furthermore, the average figure of resistant isolates for clarithromycin was 28% in Pfizer's study which fell very much into line with Abbott's recent promotional item for Klaricid (clarithromycin) (ref PXKLT 95165).

Following preliminary consideration by the Code of Practice Panel, Pfizer had been asked to provide more information about the NCCLS and BSAC breakpoints and to provide photocopies of relevant extracts from appropriate materials. Pfizer had also been asked to respond in more detail to the comments made by Abbott with regard to the erythromycin breakpoint being to the left of the normal distribution, the clarithromycin breakpoint used being positioned over the peak whilst the azithromycin breakpoint used was placed to the right of the mode. It appeared that there was more data relating to this than had been provided to the Authority. Pfizer was also asked to clarify its reference to 28% being in line with Abbott's recent Klaricid promotional item as this figure did not appear in the Abbott item where the Panel could only find a statement that *Haemophilus influenza* was greater than 75% sensitive to Klaricid.

In response, Pfizer said that the BSAC method for obtaining breakpoints was dependent on a formula which took into account a number of variables. The concentration maximum of the drug was multiplied by its degree of protein binding which was then divided by three variables; firstly the half life of the drug, secondly, a factor to ensure that the reproducibility of the results was satisfactory and help define the range for the minimum inhibitory concentration (MIC), as well as a further factor to allow for the time which the drug's concentration exceeded the MIC.

When this formula has been applied, it allowed a breakpoint to be calculated and this in turn determined where on the normal distribution curve the breakpoint was situated: be it to the left of the normal distribution in the case of erythromycin, over the peak in the case of clarithromycin and to the right of the mode in the case of azithromycin.

In relation to the Abbott promotional material for Klaricid, this said that more than 75% of *H. influenza* organisms were sensitive to clarithromycin and it would therefore seem that approximately 25% could be expected to be resistant.

RULING

1 The independent expert adviser consulted by the Authority had stated that it may be difficult to devise breakpoints, particularly when the MICs for a collection of strains fell in a single continuous distribution, rather than a biomodal distribution. This was the situation with these three macrolides and *H. influenza* and this made the choice of breakpoints contentious. Abbott seemed to suggest that the breakpoints were chosen simply on the basis of the *in vitro* behaviour of the bacteria - to separate natural populations of strains, but this was not so. The breakpoints were based on the concentrations of the drug obtained in the body. Without this element of interpretation, the basic MIC values and the comparison of these were meaningless. Pfizer had selected breakpoints from the most reputable authorities in the UK and the USA. The NCCLS system in the USA had a pharmaceutical company contribution to the debate before a breakpoint was chosen. The NCCLS methods were almost mandatory in the USA and the NCCLS breakpoints would be applied almost universally so that these were the criteria used to divide strains into "sensitive" and "resistant" - for example, in informing clinicians about strains from individual patients.

The adviser had noted, however, that although in its response Pfizer quoted concentration breakpoints as applied to MIC results, in fact it used a disc-diffusion method in its study. For the interpretation of its results, it used the criteria for the diameter of the zone of inhibition produced by a disc of defined concentration of antibiotic. These criteria, quoted by the NCCLS in the table provided, were equivalent to the concentration breakpoints. There were, however, two problems.

Firstly it was not clear from where the erythromycin zone breakpoint was derived as the BSAC source did not give criteria in these terms. Attached to the protocol for the study was a diagram in which inhibition zone diameters (round erythromycin 5ug discs) were compared with the BSAC working party concentration break point of 0.5mg/l. The provenance of this diagram, the key to the symbols and the growth medium used were not given.

Secondly, the USA NCCLS was insistent that the breakpoint criteria quoted applied only to a particular culture medium. This was not used in the Pfizer study. To justify using the NCCLS criteria, Pfizer should be able to show that these criteria were valid with the medium that it actually used in the study (as might well be so). Had the study been submitted for publication, this anomaly would have been investigated. It was a pity that the claims were based on a study which had not been subject to reviewers' and editors' scrutiny.

Once the zone breakpoints were accepted, the analysis carried out and presented - of the numbers or proportions of strains sensitive or resistance to each antibiotic - was entirely conventional. Although this simple statement hid considerable doubt and complexity, it was difficult to think of another mode of expression that would be helpful to the general reader.

The adviser had concluded that it had not been wrong of Pfizer to adopt the breakpoints recommended by the standard authorities in order to interpret results of an *in vitro* study and for it then to express the results as it had done. On the other hand, Pfizer could be criticised for the

use of inhibition zone diameter breakpoints in conditions for which these were not intended (unless Pfizer had further data to show that the substitution of the different medium did not make any significant difference).

The Panel accepted the view of its adviser that it had not been wrong of Pfizer to adopt the chosen breakpoints and ruled that there had been no breach of the Code.

2 In relation to the Zithromax card, the Panel noted that the data were clearly and prominently labelled as *in vitro* data. It was stated that *in vitro* data may not correctly translate into "clinical results" though this was in very small type. The much more prominent headline was "Zithromax - a macrolide with a difference in bronchitis".

The Panel considered that it was not sufficiently clear on the card that the *in vitro* data might not be correctly translated into clinical results. The limitations of the data had not been made clear and readers would be encouraged to extrapolate the *in vitro* data to the clinical setting. The Panel considered that the card was misleading and therefore ruled a breach of Clause 7.2 of the Code.

In the journal advertisement, the data were again clearly and prominently labelled as *in vitro* data and it was stated that "*In vitro* data may not directly translate into clinical results", this time in somewhat larger type. No clinical condition was mentioned in the headlines where the only claim was bacteriological efficacy against *H. influenza*. The Panel considered that the piece did not encourage extrapolation to the clinical setting and ruled that there had been no breach.

In relation to the brochure, the Panel considered that this was effectively a summary of study results. The data was clearly and prominently labelled as *in vitro* data. No clinical condition was mentioned. In the Panel's opinion, the piece did not encourage extrapolation to the clinical setting and accordingly ruled that it was not in breach.

3 The Panel noted that it had ruled under 2 above that there was no implication of clinical significance of the *in vitro* data in relation to the journal advertisement or the brochure. In view of this, these were considered not to be in breach in relation to this allegation either. There was a clinical claim on the card but this was for bronchitis which was a licensed indication for Zithromax. The Panel considered that this was not unacceptable.

The Panel accordingly ruled that there had been no breach of the Code in this regard.

The Panel noted that the card had been ruled in breach of Clause 7.2 in point 2 above.

4 The card did not appear to the Panel to refer to the interim data at all. In the journal advertisement, the results were clearly presented in sufficient detail to be interpreted and they were sufficiently supported by the "data on file" referenced. The Panel considered that the data could not be considered misleading in themselves. In relation to the brochure, again the results were presented in sufficient detail to be interpreted and again the Panel considered that they could not be considered misleading in themselves.

The Panel noted that the final data were apparently not significantly different from the interim. Although the Panel had some reservations on the matter, on balance it did not consider in the circumstances that it was misleading to fail to state that the data presented were interim and accordingly ruled that there had been no breach of the Code.

Complaint received **2 August 1995**

Case completed **5 January 1996**

CASES AUTH/336/9/95 & AUTH/370/11/95

SCHERING HEALTH CARE/MEDICINES CONTROL AGENCY v SERONO

Advance information about an unlicensed product, interferon beta-1a

Schering complained about a brochure and letters issued by Serono in relation to the provision of advance information about the introduction of interferon beta-1a, alleging that the information went beyond that permitted by the ABPI Guidelines on advance notification of new products and was in breach of Clause 3.1 of the Code. It was also alleged that there was a breach of Clause 8 because the material inferred that clinicians would overprescribe interferon beta-1b when that shortly became available.

The Medicines Control Agency (MCA) subsequently referred to the Authority a complaint it had received about the same material. The material seemed to the MCA to be unnecessarily comprehensive simply to provide advance information in line with the ABPI Guidelines.

The Panel considered that too much information had been provided. Too much detail had been given about the differences between interferon beta-1a and 1b and use of the former positively advocated. A breach of Clause 3.1 was ruled. The Panel did not consider that there had also been a breach of Clause 8. Upon appeal by Serono, the Appeal Board decided that the mailings sent out by Serono went beyond what was acceptable and upheld the Panel's ruling that there had been a breach of Clause 3.1.

Case AUTH/336/9/95

COMPLAINT

Schering Health Care Limited complained about a brochure on beta interferon-1a and multiple sclerosis which had been produced and distributed by Serono Laboratories (UK) Ltd. Schering said that ostensibly the brochure was intended to inform purchasers and advisers about interferon beta-1a. Schering believed that the brochure far exceeded the ABPI Guidelines on advance notification of new products, referred to in the supplementary information to Clause 3.1, and the brochure therefore constituted a breach of Clause 3 of the Code.

Schering alleged that the material presented in the brochure was clearly promotional in content and was presented in the style of a promotional piece. The covering letter also contained several promotional statements. The brochure contained not only information relevant to interferon beta-1a but also a great deal of information about interferon beta-1b. This clearly invited promotional comparisons between the products with respect to chemical structure, side-effect profiles and evidence of efficacy. Clinical results of an unpublished open trial with no placebo comparator were presented to support the use of interferon beta-1a and were followed by extensive details of Serono's ongoing trial programme which seemed irrelevant for the presumed target audience. Guidelines for patient selection pre-treatment were presented with no clear reference made to the fact that these were developed by the American Academy of Neurology to support the use of interferon beta-1b, not beta-1a, based on the results of the interferon beta-1b pivotal trials. Speculative reference was made to the potential cost benefits for arresting disease progression when there was no evidence that interferon beta-1a could achieve this goal.

Schering considered that it was clearly a promotional brochure which attempted to do much more than simply inform hospital authorities of the facts about beta-1a.

Schering further complained in a subsequent letter about a letter entitled "The managed entry of beta interferon-1a in multiple sclerosis" which had been distributed by Serono as a follow up to the previous piece. This letter also contained several promotional statements and invited promotional comparison between interferon beta-1b and 1a. As such, it was in breach of Clause 3 of the Code. Reference was made in the letter to outdated guidelines from the Association of British Neurologists (ABN) and there was an inference that clinicians would be over prescribing interferon beta-1b once it became available. Schering had been working closely with the Department of Health to manage the introduction of interferon beta-1b and these disparaging references were in breach of Clause 8 of the Code.

RESPONSE

Serono commented separately in relation to the two mailings.

1. Recombinant beta interferon-1a in multiple sclerosis (MS) (Ref 1OO3/07/95, 1OO2/04/95)

Serono said that the brochure was developed specifically to inform purchasers and advisers about a forthcoming new medicine. This was in line with requests that information on new medicines, particularly those which might have significant financial implications, should be provided to budget holders well before the medicine received marketing authorization. The item was developed as a single mailing to be sent to directors of public health, medical and pharmaceutical advisers to FHSAs, DHAs, HCs and chief pharmacists in provider units. It was not sent to prescribers such as neurologists. This non promotional advance information was developed in accordance with the ABPI Guidelines. Serono's recombinant beta interferon-1a (Rebif) was still more than twelve months from a likely date of licensing.

The brochure set out factual scientific information on Serono's compound, recombinant beta interferon-1a, and another recombinant beta interferon-1a (Biogen) and recombinant beta interferon-1b (Schering). No comparisons were drawn between the compounds. The information was presented in order that purchasers could plan accordingly.

In relation to Schering's particular points, and dealing first with promotional content and style, Serono said that the brochure in question was produced with a black and white body copy and no visuals specifically so it would not be seen as promotion. It was clearly marked as a review for purchasers and advisors and was never sent to neurologists.

In relation to the provision of information on beta inteferon-1b, Serono said that rather than inviting promotional comparison, this information was included to give purchasers a full view of the beta interferons and to clarify the considerable confusion which Serono had experienced among purchasers about 1b and 1a.

In relation to Schering's comments about clinical results, Serono said that the clinical results which were presented on beta interferon-1a were two studies in particular, both of which had been presented to international meetings and submitted for publication. The first study was presented by Jacobs *et al* at the American Neurological Association and was a placebo controlled study of Biogen's recombinant beta interferon-1a involving 301 patients. The second study which was presented on recombinant beta interferon-1a used Serono's compound and compared two dose schedules. The design involved a six month observation period followed by a six month treatment period randomly assigned to three or nine MIU three times a week.

Schering was also concerned that Serono had given an overview of its ongoing clinical trial programme. Serono said that the reasoning behind this was to address questions that it had received concerning the role of beta interferons in the other types of multiple sclerosis (MS). Although Schering's compound was licensed in the US for relapsing, remitting MS, there was considerable interest in treatment for other groups which would have major resource implications for health authorities. Serono's trial programme involved secondary progressive and early onset, in addition to relapsing, remitting MS. Details of the programmes were given because of criticism of the size and design of some earlier studies in the field. The section on guidelines for patient selection was clearly referenced as being derived from advice given from the Advisory Committee to the American Academy of Neurology and published in "Neurology" in 1994.

In relation to the arrest of disease progression, Professor McDonald had indicated in an article in the British Medical Journal that treatment with recombinant beta interferon-1a might have a favourable effect on the course of the disease. It would seem a reasonable supposition that arresting disease progression could save money.

2 The managed entry of beta interferon-1a in multiple sclerosis (Ref 1O14/09/95)

Serono said that this letter had been sent out following a clinical investigator meeting when it identified a need for a national study looking at disability, cost benefit and quality of life. It was not a follow up to the previous piece, as Schering suggested. Serono's discussions with clinicians and purchasers led it to believe that there was a need for longer term disability data than was currently available, or being collected. The purpose of the letter was, therefore, to invite purchasers to attend the meeting to discuss the concept of a collaborative project managing the entry of beta interferon-1a in the context of a longitudinal cohort follow up study.

The information contained was purely factual in order for recipients make a decision concerning attending the meeting. Serono was interested in Schering's comment about the ABN guidelines. To Serono's knowledge these were the current versions. Further guidelines were in preparation but were not yet available.

In relation to the inference that clinicians would over prescribe beta interferon once it became available, Serono submitted that if this sentence was taken in context it was actually discussing the point that the appropriate treatment should go to the right patients. Serono certainly did not see this sentence as being disparaging to Schering's activities. Indeed, Professor Walley, in his recent BMJ paper, reviewed options for the introduction of beta interferon, including the potential for widespread prescribing. The same considerations had been reported by purchasing health authorities across the UK.

PANEL RULING

The Panel noted that the guidance on the question of advance notification of products which did not yet have a licence issued by the The Association of the British Pharmaceutical Industry (ABPI) in 1992 applied, *inter alia*, to products which contained a new active substance or a newly synthesised active substance. Among the conditions were that the introduction of the product had to have significant budgetary implications, the information had to be provided well ahead of the launch date and it had to be directed to those concerned with budgets and not to those who would be expected to prescribe the product. The Panel considered that these particular conditions had all been met by Serono.

The question to be addressed by the Panel was whether a further condition in the guidelines had also been met, that was to say that only factual information could be provided, including an indication of the likely cost and that it could not be presented in the style of promotional material.

The Panel noted that the printed brochure which had been provided was entitled "Recombinant beta interferon in the treatment of multiple sclerosis. A review for purchasers and advisers." It was not presented in the relatively flamboyant and colourful style generally adopted for promotional material but, on the other hand, neither was it without promotional overtones. The cover was printed in two colours, the contents were printed in black, and a stylised "beta" appeared on the cover and on every single page in the brochure. The brochure had been sent out in a folder together with a detailed letter and a number of clinical papers.

The printed brochure had been accompanied by the letter entitled "Recombinant beta interferon-1a in multiple sclerosis (MS)", a postcard to allow further information to be requested and five reports of clinical studies. The second letter entitled "The managed entry of beta interferon-1a in multiple sclerosis" had been accompanied by four reports of clinical studies and by a document dated 22 November 1994 which stated that it was the official position of the Association of British

urologists on beta interferon and Copolymer -1 in the treatment of multiple sclerosis. Although Serono had stated that the second letter was not a follow up to the first letter, the Panel noted that the second letter did refer to the first.

The Panel observed that it was a contravention of Clause 3.1 of the Code to promote an unlicensed medicine and that the guidance on advance notification of new products which did not have a licence was intended to allow a limited amount of factual information as to the use of a product to be provided to those concerned with budgets and the like so that they could take account of the forthcoming introduction of the product in question and its likely budgetary implications. It was not intended, nor could it be regarded, as opening a door through which any amount of unsolicited information could be provided.

The Panel considered that too much had been provided in both the first and second packages of information. The use of the product was positively advocated and it was compared favourably with other similar products. Too much detail had been given about the differences between beta interferon-1a and 1b and about the clinical trial programme. The material went beyond that permitted and the Panel ruled that there had been a breach of Clause 3.1 of the Code.

If recipients of permissible information had asked Serono for further details, the Panel considered that it would have been acceptable for Serono to have supplied more information at that stage and have remained within the Guidelines.

The Panel did not accept that the second mailing inferred that clinicians would be over prescribing beta interferon-1b once it became available as alleged. The reference to widespread prescribing was considered to be a reference to beta interferon in general. The Panel did not accept that the material was disparaging and ruled no breach of Clause 8 of the Code.

Case AUTH/370/11/95

A further complaint about the same material was passed on to the Authority by the Medicines Control Agency (MCA). The MCA noted that the product did not have a marketing authorization and nor had an application yet been made to the MCA. Promotion of an unlicensed medicine was an offence under Regulation 3 of The Medicines (Advertising) Regulations 1994 (SI1994 No1932). The complainant to the MCA was concerned about this form of publicity and considered it to be misleading. While the material was not directly promotional, it did seem to the MCA to be unnecessarily comprehensive simply to provide advance information of a product in line with the ABPI Guidelines.

The Panel considered that this complaint was essentially the same as that in Case AUTH/336/9/95 and advised Serono that the ruling in that case would also apply in Case AUTH/370/11/95.

Serono appealed the Panel's ruling of a breach of Clause 3.1 of the Code in both cases.

APPEAL BY SERONO

Cases AUTH/336/9/95 & AUTH/370/11/95

Serono said that the Panel's ruling related to two separate communications addressed to purchasers and advisers by Serono. The first was intended to inform purchasers about a type of multiple sclerosis therapy, recombinant beta interferon-1a, which might be relevant to their deliberations when estimating likely budgets two of more years in advance. The second letter was specifically to invite purchasers to attend a meeting to discuss their needs in terms of managing the entry of beta interferon and the possible requirement for a long term disability study.

Serono's view was that the documents complained of were not promotional. They were developed specifically to provide purchasers and advisers with advance notification about the qualities of this type of therapy in accordance with the ABPI Guidelines on advance notification of new products or product changes.

Serono noted that the Panel had considered that all of the conditions of the Guidelines had been met except for:

"Only factual information must be provided, including an indication of the likely cost, and it must not be presented in the style of promotional material;"

Serono asked that the Panel's ruling of a breach of Clause 3.1 be reconsidered in the light of the following points which were intended to address the Panel's concerns.

"The Panel considered that too much had been provided in both the first and second packages of information"

The documents comprising the first "package of information" sent out in August 1995 were the booklet headed "Recombinant beta interferon in the treatment of multiple sclerosis - A review for purchasers and advisors" and a covering letter headed "Recombinant beta interferon-1a in multiple sclerosis (MS)". The second "package", sent out in late September 1995 comprised one letter headed "The managed entry of beta interferon-1a in multiple sclerosis"; this concerned Serono's proposal for a meeting.

Serono did not believe that the use of the expression "package" to refer to what the purchasers would have received was fair or accurate but it used that term simply for consistency.

The Panel's ruling referred to papers of clinical studies having been enclosed with each package. Serono wanted to clarify at the outset that no clinical papers or studies were sent to purchasers and advisers: they were referenced in both of the letters and the brochure but were not provided. Serono had supplied the Panel with all of the references and enclosures as requested by the Authority.

"The use of the product was positively advocated and it was compared favourably with other similar products"

Serono presumed the Panel to mean that the use of recombinant beta interferon-1a was positively advocated and was compared favourably with recombinant beta interferon-1b. However, the level at which the documents operated was at the level of the type of treatment, and not the level of the specific product.

To explain this point, Serono emphasised a fact which it was not sure that the Panel appreciated, that there were two separate recombinant beta interferon-1a products within the 1a type. One was manufactured by Serono and the other by Biogen. If the Panel did appreciate this fact, its ruling did not indicate so as the ruling referred to the "use of the product".

The information packages complained of comprised scientific factual information about alternative "potential" therapies in the treatment of multiple sclerosis, recombinant beta interferon-1a and recombinant beta interferon-1b. The review and the two letters referred to three studies, one on recombinant beta interferon-1b and two on recombinant beta interferon-1a. Attempts to draw the reader's attention to a particular product were studiously avoided.

The material complained of did not identify any one product in the range of therapies because it was produced to provide advanced notification to purchasers, in accordance with the ABPI Guidelines, of budgetary considerations which might be thought relevant, as a matter of general interest, in the introduction of recombinant beta interferon-1a. It was important for the purpose of the appeal to repeat that the first study of recombinant beta interferon-1a referred to in the review for purchasers and advisers was a study of Biogen's recombinant beta interferon-1a; the second was a study of Serono's compound.

Schering complained of comparisons in Serono's information packages of chemical structure, side effect profiles and evidence of efficacy. Serono disagreed that comparisons were made but noted that the documents complained of presented factual information from which comparisons could be drawn.

With regard to chemical structure, Serono disagreed that any comparison which could be made was favourable to either interferon-1a or interferon-1b. The chemical structure was simply different. However, insofar as there was any comparison to be drawn between types of treatment, Serono failed to see the promotional content. The significance of the comparison lay in the purchasers' conclusions as to how these differences might affect budget estimates which in Serono's view underscored the basis of the Guidelines.

None of the material was intended to be promotional. Further, Serono disagreed that the material was promotional in style or in content. The term "promotion" was defined in Clause 1.2 of the Code which provided (*inter alia*) that promotion does not include "factual, informative announcements ... provided they include no product names". In Serono's view, the materials were no more than factual informative annoucements. Serono never intended to make, and did not believe that it did make a "product claim" about a Serono product.

Serono made available a copy of a letter which it had received from a family health services authority concerning the need for full information about forthcoming products.

"Too much detail had been given about the differences between beta interferon-1a and 1b and about the clinical trial programme"

The reasons information was provided about the difference between recombinant beta interferon-1a and 1b and why detail was provided about Serono's ongoing clinical trial programme had been provided to the Panel. To reiterate, Serono had formed the judgement that if sufficient information was not provided, the target audience would remain confused about the different types of therapeutic agent available and the purpose of the material was to inform. From numerous enquiries Serono had received and continued to receive each month, Serono was aware of considerable uncertainty about the beta interferons. The information provided was intended to clarify. The reasoning behind providing an overview of Serono's ongoing trial programme was to address questions that it had received concerning the role of beta interferons and the other types of MS. Although Schering's compound was licensed in the USA for relapsing, remitting MS, there was considerable interest in treatment for other groups which would have major resource implications for health authorities. Serono's trial programme involves secondary progressive and earlier onset, in addition to relapsing, remitting MS. Details of the programmes was given because of criticism of the size and design of some earlier studies in this field.

Serono commented further that Schering's complaint was based, in part, on Serono's reference to the clinical results of an unpublished trial. In fact, the review for purchasers and advisers referred to two as yet unpublished clinical studies which had been presented at international conferences and hence were in the pubic domain. Serono did not believe it could have made it clearer than it did that the studies referred to were not published.

At the time Serono considered it appropriate to provide advance notification to purchasers about recombinant beta interferon-1a in accordance with the ABPI Guidelines (which required that information was provided "well ahead of the product launch ... normally not less than one year before the expected date"), there were no published studies on the 1a type of interferon. Serono took the view that if it delayed notification pending publication of such studies, it risked not being able to give advance notification within the one year period specified in the guidelines.

As Serono was unable to refer to published studies, it considered that information about its ongoing clinical trial programme should be included in the information package in order to establish an element of clinical credibility with purchasers and advisers.

APPEAL BOARD RULING

The Appeal Board noted that, as had been clarified by Serono, the first letter had been accompanied only by a printed brochure entitled "A review for purchasers and advisers" and by a reply paid card for requesting further information. The second letter referred to the first letter and had been accompanied only by a response sheet. The papers in each instance had not been dispatched in the folders with which the Panel had been provided by Serono and which had included the various scientific papers etc. Serono had sent all of these papers to the Panel for its information but they had not actually been sent to recipients of the letters.

The Appeal Board noted that although the ABPI Guidelines on advance notification had been issued in 1992, this was the first complaint about such guidance which had been received and its decision would be an important precedent.

The Appeal Board considered first the appearance of the brochure entitled "A review for purchasers and advisers". It noted that this was presented with some style as to typography etc but with colour being used only on the front cover. The Appeal Board considered that it was quite acceptable for advance information to be presented in a readily readable and attractive form, provided that it did not have the appearance of promotional material. Good presentation made a document easier to read and more likely to be read. Restraint needed to be exercised, however. In this particular instance, the Appeal Board considered that the presentation and appearance of the brochure was close to the limits of acceptability in relation to the requirement in the ABPI Guidelines that information must not be presented in the style of promotional material. The Appeal Board decided, however, that this requirement of the Guidelines had been met with regard to the appearance of the brochure but was nonetheless of the opinion that logos should only appear on such material if they were company associated logos and not related to any product.

As to the actual content of the materials which had been provided, the view of the Appeal Board was that the overall impression to be gained by a reader of the brochure was that Serono's as yet unlicensed product was superior to the beta interferon-1b product about to be licensed and that potential purchasers should take account of that fact.

In the brochure, there was considerable information about beta interferon-1b, a whole page being devoted specifically to it in addition to references to it elsewhere. Common side-effects were tabulated which gave them emphasis whereas those for beta interferon-1a were given in the text. The Appeal Board considered that the information provided should have related to beta interferon-1a without unfavourable comparisons being drawn in respect of beta interferon-1b. The Appeal Board considered that the brochure was promotional in content whatever the intentions of Serono had been.

The Appeal Board considered that both mailings sent by Serono went beyond that which was acceptable and upheld the Panel's ruling that there had been a breach of Clause 3.1 of the Code.

The appeal therefore failed.

Complaints received

Case AUTH/336/9/95 **25 September 1995**

Case AUTH/370/11/95 **13 November 1995**

Cases completed **8 January 1996**

CASE AUTH/338/9/95

PHARMACEUTICAL ADVISER TO HEALTH BODY v GLAXO

Zantac detail aid

A pharmaceutical adviser to a health body complained about a detail aid issued by Glaxo which discussed a particular FHSA in relation to gastrointestinal drug costs and reducing Zantac prescribing.

The Panel ruled that a bar chart showing changes in total gastointestinal drug costs and changes in expenditure on Zantac was misleading as it was not adequately labelled so that the limitations of the data could be assessed. The Panel also ruled that the use of the word "many" in relation to 9 out of 74 (12%) patients dissatisfied with a switch from Zantac to nizatidine was misleading. These rulings were accepted by Glaxo.

The Appeal Board upheld the Panel's rulings of no breach with regard to three allegations which were appealed by the complainant. These related to, firstly, the phrase "uncertain cost savings" used to describe the costs associated with patients dissatisfied when switched from Zantac to nizatidine which was alleged to be misleading. Secondly, a claim "The pressure by Wirral FHSA to reduce Zantac prescribing has not reduced overall costs" which was alleged to be misleading and disparaging. Thirdly a graph showing increasing sales in the acid suppressant market and decreasing sales of Zantac which was alleged to be misleading and unbalanced.

The complaint concerned a detail aid issued by Glaxo Pharmaceuticals UK Limited. The detail aid was headed "Does cutting Zantac usage cut gastrointestinal drug bills?" and included a bar chart headed "Change in total gastrointestinal drug costs and Zantac costs" which compared the change in total gastrointestinal drug costs to the change in expenditure on Zantac (ranitidine) for four family health service authorities (FHSAs); Wirral, Liverpool, St Helens and Sefton. The detail aid then referred to an audit of five general practices and presented information from the audit of over 200 patients with symptoms satisfactorily controlled on Zantac which were switched to nizatidine solely to save costs.

Page 3 of the detail aid was headed "The pressure by Wirral FHSA to reduce Zantac prescribing has not reduced overall drug costs" beneath which a graph headed "Wirral FHSA IMS sterling sales" compared IMS sterling sales of Zantac with the acid suppressant market. In the graph the sales of acid suppressants were shown as rising whereas the sales of Zantac were decreasing. The graph was followed by a claim "Clearly Zantac is not contributing to these increasing drug costs".

COMPLAINT

A pharmaceutical adviser to a health body complained

about the detail aid which she believed had been used during the summer around the country with general practitioners. The complainant was concerned that the data itself and the way it was presented gave an extremely misleading picture of the facts.

The bar chart entitled "Change in total gastrointestinal drug costs and Zantac costs" showed Wirral with the greatest growth in total gastrointestinal drug costs (15.4%) and the largest reduction in Zantac expenditure (20%) of the Mersey FHSAs shown and Sefton with second highest growth in GI drug costs (14.5%) and second largest reduction in Zantac costs (9.5%). The complainant considered that anybody reading the material might be forgiven for thinking that there could be an inverse relationship between growth of GI costs and change in Zantac expenditure and therefore it might be counterproductive to change from Zantac.

The complainant referred in detail to confidential PPA PACT data which showed a different picture to the data shown in the detail aid.

The complainant alleged that the bar chart in the detail aid was in breach of Clause 7.2 as comparisons must be accurate, unambiguous and must not mislead. It was unclear what "total gastrointestinal drug costs" constituted. The complainant had tried various permutations using PPA PACT data and could still not produce the same or similar relative pattern between the FHSAs to that given in the detail aid. The complainant found the opposite of what was shown in the detail aid with regard to gastrointestinal drug growth comparison between the given FHSAs. The complainant was unclear as to what was meant by MAT February 1994 - January 1995" which appeared beneath the bar chart.

The complainant alleged that the information concerning the audits conducted in five general practices which appeared in the detail aid as a series of bullet points was misleading. The complainant believed these were conducted by a doctor on Glaxo's behalf and were the subject of a letter in Update 1 June 1995. The complainant pointed out that the Update letter stated that 217 patients were studied each receiving equivalent doses of nizatidine and of these 143 (66%) were satisfied with the change. This could therefore produce significant cost savings because of the lower price of nizatidine, particularly as it was also indicated that of the 74 (34%) not satisfied with the change, the majority (62) were returned to ranitidine (so no higher cost than before). The detail aid emphasised the number not satisfied with the switch even though this was a lesser number than those who were satisfied. The detail aid also stated "The majority of dissatisfied patients were switched back to Zantac, although many were prescribed a more expensive acid suppressant". In the complainant's view the use of the word "many" was misleading as seven patients were given omeprazole and two a higher dose of nizatidine. These small numbers did not constitute "many". The statement was trying to give an impression that such a switch might be counterproductive in terms of making savings as patients might be switched to more expensive acid suppressants. This was not supported by the information given as even if one assumed that all the patients changed to omeprazole were given a 40mg dose, which was unlikely, this would not negate savings resulting from the switch overall. However the detail aid referred to "uncertain cost savings".

The complainant drew attention to another statement in this section of the detail aid that "Over one third of patients were dissatisfied, mainly because their acid-related symptoms were no longer under control". This was alleged to be misleading as the patients in the audits were not part of a controlled clinical study which could establish this one way or another. Even the Glaxo letter in Update acknowledged this by stating that "the majority of patients who were dissatisfied claimed that their symptoms were not controlled" and that "a difference in efficacy cannot be excluded. Alternatively the perceived differences between ranitidine and nizatidine may result from a placebo effect".

The complainant referred to the next page in the detail aid headed "The pressure by Wirral FHSA to reduce Zantac prescribing has not reduced overall drug costs" and alleged that the use of the word "pressure" implied a negative image somehow forcing or coercing GPs to do something which was certainly not the case. It was misleading and disparaging and did not give a fair description of what was in fact an FHSA properly discharging responsibilities around improving cost effective prescribing through professional advice. A breach of Clause 8.2 was alleged.

The complainant alleged that a graph appearing on the same page headed "Wirral FHSA IMS sterling sales" was misleading and not balanced as it did not give a comparison with the overall rate of growth for any other district or the England average. The complainant provided a chart demonstrating how Wirral had improved its position around the regional average in comparison with other Mersey FHSAs. This had been achieved by slowing down the cost growth by cost effectiveness improvements including the switch to nizatidine. One would not reasonably expect a reduction in expenditure for this category in absolute terms and so the heading "...has not reduced overall drug costs" was misleading. Therefore once again GPs reading the detail aid might be forgiven for concluding that changes on the Wirral had been unsuccessful and even counterproductive when in fact the complainant's estimate of the savings attributable to the nizatidine switch were in the order of £150,000 over two years. The increase in proton pump inhibitors spend did not appear to have been accelerated by the nizatidine switch as implied by the detail aid. The complainant provided data to support this point.

Finally the complainant had never seen a detail aid featuring an FHSA's prescribing before and questioned the appropriateness of this. The company at no point consulted with the FHSA regarding display of Wirral prescribing figures in the detail aid. The fact that it was being used in other parts of the country and was also giving a misleading impression to GPs and others as to what had happened in Wirral gave the complainant further concern.

RESPONSE

Glaxo advised that the detail aid was used by representatives to explain the situation to doctors only in the Wirral area. It was not used with GPs around the country although other similar material was used in other areas.

The detail aid in question was produced and the audit carried out because many GPs in the area did indeed feel under pressure from the FHSA to change patients from Zantac to nizatidine, not on clinical grounds but entirely to save money because nizatidine was cheaper.

Glaxo pointed out that the detail aid claimed that reducing the amount of Zantac did not necessarily cut the gastrointestinal drug bill according to the data presented in the detail aid. The company had used data that was available within the public domain and figures were based on the British Pharmaceutical Index (BPI) (IMS data source). IMS was a well established and respected provider of data for the whole of the pharmaceutical industry. The BPI data was based on 97% of all sales to retail and doctor outlets which was received from wholesalers and manufacturers as census data. The residue of the market, approximately 3% was estimated from the purchase data of 850 chemist shops.

The company was not privy to the PPA PACT data on which the complainant had based her allegations. The company submitted that the fundamental issue was the discrepancy between BPI data and PPA PACT data. The discrepancy could be because BPI data was based on retail and doctor outlet sales, whilst the PPA PACT data was based on actual GP prescribing.

The company listed the products included in IMS "Total Gastrointestinal Drug Costs" and in the BNF 1.3 "Ulcer Healing Drugs". The categories overlapped except that the IMS list included Gaviscon and Maxolon which were not in the BNF section 1.3 and the BNF section 1.3 included pirenzepine which was not on the IMS list. The company had analysed the BPI data using the BNF 1.3 Ulcer Healing Drugs list, and stated that the difference was not significant.

Glaxo submitted that many FHSAs were urging GPs to switch patients from Zantac to cheaper nizatidine in order to save money without giving consideration to the proportion of patients who for whatever reason would be dissatisfied with the change. It was common sense that a proportion of patients would be dissatisfied and would require further consultation, further prescriptions and might even finish up on more potent or more expensive treatment. The results of the audit conducted in general practices were presented in the detail aid to illustrate these points. In this particular audit, 34% were not satisfied with the change and, although returning to original treatment, would have incurred the expense of wasted prescriptions and return visits which, contrary to what the complainant stated, must incur extra costs.

In addition many patients in the audit (greater than 12% of those who were dissatisfied) finished up with more potent acid suppression. Glaxo submitted that 12% was more than a "few" and less than "most" so "many" was an appropriate description. Again it was merely intended to make individual GPs consider the possibility that many of their patients could finish up on more potent acid suppressants if they undertook such a policy. Given the uncertainty of the outcomes of such policy, Glaxo submitted that it was justifiable to claim that the cost savings would also be uncertain and not as clear as the simplistic calculations made by many FHSA advisers whose figures were often derived from assumptions that all Zantac prescriptions were satisfactory replaced by nizatidine. Such assumptions were based on cost alone with no factual data to support them. There were no comparative studies between ranitidine and nizatidine in non ulcer conditions.

With regard to the allegation that it was misleading to present the data on patient satisfaction with treatment change on the grounds that it was not a controlled clinical trial, the company pointed out that it was clearly stated that the data was from an audit. The purpose of the audit was to see what happened in real clinical practice and not the artificial clinical trials situation. The audit recorded the subjective feelings of individual patients towards the change of treatment and, in those who were dissatisfied, their reasons for believing it was not satisfactory. As stated by the complainant this could be due to true differences in efficacy or the results of a placebo effect. Nevertheless the point was that a significant proportion of patients were dissatisfied for whatever reason.

Glaxo submitted that the repeated mailing and visiting of GPs in an attempt to change prescribing could be fairly described as "pressure ...to reduce Zantac prescribing" and that this description did not intentionally or inadvertently disparage the clinical and scientific opinions of the complainant or colleagues.

The detail aid claimed that Zantac was not contributing to the increase in Wirral GI drug costs. Since the Zantac sales were decreasing there it appeared to be a valid claim. The relative growth rates of Wirral's costs and the costs of other areas were not directly relevant to the claim. The complainant referred to a graph depicting cost variances to support the view that Wirral's growth of total GI drug costs had been curbed by the switch from Zantac. It was not stated what the variances were and it was impossible to ascribe much meaning to them. In any case they probably depended on data that was not in the public domain.

The company submitted that it had tried to clarify further the situation regarding the growth rates of total GI drugs spend in Wirral as compared to other FHSAs in Mersey by using BPI data which was in the public domain. A graph was provided which compared the moving annual total growth rate of the total GI market (IMS data sterling sales) for Wirral FHSA, other Mersey FHSAs and nationally. The company had computed the moving annual total spend, month by month, and also the monthly rate of growth of that. The figures showed that the rate of growth in Wirral had been generally higher than in other Mersey FHSAs. The Wirral figures were generally comparable to the national picture, but the comparison of the three local areas was surely more telling.

PANEL RULING

The Panel considered that as a matter of principle it was acceptable for companies to refer to data relating to individual FHSA areas and to respond to information etc distributed by FHSAs and other bodies provided that it was done in such a way as to comply with the Code. The Panel considered that it was acceptable in principle for Glaxo to refer to the effects of reducing the use of Zantac in the FHSA areas stated in the detail aid. It noted Glaxo's submission that this particular detail aid had not been used nationally. Its use had been restricted to Wirral FHSA.

With regard to the bar chart, the Panel noted that Glaxo did not have access to PPA PACT data. It only had access to IMS data and had used this as a basis for the bar chart. In the Panel's view it was not necessarily acceptable for Glaxo to use IMS data on the basis that it was the only data available. The use of any data would have to be justified and account would have to be taken of the claims etc based on the data used.

The Panel noted that the two data sets differed in a number of respects. Firstly, the IMS data was based on sales whereas the PPA PACT data was based on actual prescribing. Secondly, there was a discrepancy between the products included in the IMS "Total Gastrointestinal Drugs" and in the BNF section 1.3 "Ulcer Healing Drugs" upon which the PPA PACT data was based.

The Panel noted that the data used in the detail aid was based on sales over a year. It considered that this would not be exactly equivalent to use. It would however be a reasonable indicator of use given the time period and the likelihood that stocks would remain relatively constant. It was not clear whether the sales data included sales of over the counter medicines. The data had been presented on the same bar chart which might lead doctors to conclude that the increase in total gastrointestinal drug costs was linked to the decrease in expenditure on Zantac and there was no evidence that this was so.

The Panel considered that it was not sufficiently clear from the bar chart and its labelling that the figures related to sales. The labelling of the bars as either "change in total gastrointestinal drug costs" or "change in expenditure on Zantac ranitidine" were confusing given that the data was based on sales. It was likely that the reader would be unaware that "MAT" meant "moving annual total". The company should have explained the basis of the figures more comprehensively. The Panel decided that the bar chart was misleading as it was not adequately labelled so that the reader could assess the limitations of the data and therefore ruled a breach of Clause 7.2 of the Code. This ruling was accepted by Glaxo.

The Panel noted that there was no mention in the detail aid that Glaxo had been involved in the audit of patients controlled on Zantac switched to nizatidine. The letter in Update was co-authored by a general practitioner and a doctor from Glaxo. It might have been helpful to readers if this information had been given.

With regard to the presentation of the data from the audit, the Panel considered that it was not unreasonable to refer only to the patients dissatisfied with the switch. It was also not unreasonable to use audit data in these particular circumstances. The Panel considered however that the use of the word "many" in relation to 12% of dissatisfied patients was misleading. In the Panel's view "many" would be taken to mean a reasonably substantial number of patients and not 9 patients (7 given omeprazole and 2 given higher doses of nizatidine) out of the 74 patients who were dissatisfied. The Panel therefore ruled a breach of Clause 7.2 of the Code. This ruling was accepted by Glaxo.

With regard to the phrase "uncertain cost savings" the Panel considered that there would be more costs associated with patients dissatisfied with nizatidine than simply the cost of the replacement therapy, be it Zantac or other medication. The costs of consulting the GP, wasted prescriptions etc should be taken into account when discussing savings. The Panel did not accept that the term was misleading. This ruling was appealed by the complainant.

With regard to the claim "The pressure by Wirral FHSA to reduce Zantac prescribing has not reduced overall drug costs" the Panel noted that Glaxo had referred to the repeated mailing and visiting of GPs in an attempt to encourage them to change prescribing and this could be described as pressure. It would probably be so regarded by general practitioners. That was not to say that the FHSA had acted unreasonably. The Panel also observed that the overall sales of acid suppresant drugs had increased despite the decrease in sales of Zantac. The Panel considered that it was not unreasonable to draw attention to this albeit, as submitted by the complainant, that one would not expect a reduction in expenditure for this category in absolute terms. The Panel did not accept that it was either misleading or disparaging as alleged and therefore ruled no breach of the Code. This ruling was appealed by the complainant.

With regard to the graph headed " Wirral FHSA IMS Sterling Sales", the Panel considered that it was not necessary to show a comparison with national costs. It was clear that the data related to sales although the Panel noted that it might have been more helpful if further information had been given about the data. In the Panel's view the claim below the graph "Clearly Zantac is not contributing to these increasing drug costs" was acceptable as the sales of Zantac were falling although the acid suppressant market sales were rising. It was clear the graph referred to sales and this could be taken as an indication of costs. The Panel therefore ruled no breach of the Code. This ruling was appealed by the complainant.

APPEAL BY COMPLAINANT

With regard to the claim "The pressure by Wirral FHSA to reduce Zantac prescribing has not reduced overall drug costs" the complainant pointed out that Wirral FHSA had never mailed Wirral general practitioners with regard to therapeutic substitution of nizatidine for ranitidine. Repeated visiting was in reality one or two visits a year to Wirral practices and this was an optimistic estimate. The claim gave an impression of intense activity by Wirral FHSA and it did not stand as it was factually incorrect.

The complainant stated that if the claim referring to the fact that overall acid suppressant costs were rising had been presented on its own she might agree that it was not unreasonable to draw attention to this. However it had been presented in relation to Zantac prescribing which could easily lead to the wrong interpretation. The claim could be seen as a failure of an objective if the objective was to reduce overall drug costs in absolute terms but this would not be a realistic objective of the change. A more realistic objective might be to slow down the rate of increase of prescribing costs for acid supressants. There was no way of knowing whether this had been achieved without comparator trend data for England or other local FHSAs which the complainant had previously supplied. In the complainant's view the average GP would not generally know whether achieving an absolute saving was a realistic objective or not and therefore would most probably be liable to misinterpret the claim.

The complainant queried the submission from Glaxo that the detail aid had not been used nationally and that use had been restricted to Wirral FHSA as it had been sent to her by a pharmaceutical adviser from a London FHSA. The medical adviser from that FHSA subsequently rang to ask whether the switch to nizatidine had been counterproductive for the Wirral as indicated in the Glaxo detail aid. Further a pharmaceutical adviser from a neighbouring FHSA in the north west had contacted the complainant because a general practitioner had indicated that he was not interested in considering substitution of nizatidine for ranitidine as Glaxo had indicated that the change had resulted for Wirral in an increase in prescribing costs as failures had gone on to more expensive acid supressants supposedly causing an increase in overall costs. The complainant did not know if the detail aid was used in the latter case.

The complainant said that when visiting practices a range of topics would be discussed covering a range of therapeutic areas tailored to individual prescribing patterns of the practice and issues raised by the GPs. Acid suppressants was a common area to discuss which was not surprising as it accounted for over 11% of the total GP prescribing costs and was often identified as an area where GPs felt they could justifiably make changes to prescribe more cost effectively. It was up to the practice to decide its own strategy. If a practice decided it would pursue a change in prescribing, the policy of Wirral FHSA was to encourage the practice to audit this change in conjunction with a Medical Audit Advisory Group (MAAG) to encourage a considered approach to such changes and to safeguard patient care.

The complainant referred to practice audits presented by three practices with a total of 245 patients having been changed from ranitidine to nizatidine with a pooled initial success rate of 83.3%. One of these had taken part in the Glaxo audit. In this regard the complainant stated that the Glaxo audit had given the number of patients as 22 with a failure rate of 46% whereas the GP's own audit gave the number of patients switched from nizatidine to ranitidine as 64 with a failure rate of 14%. The GP concerned suggested that one explanation for low numbers of patients indicated in the Glaxo audit might be that it had been done as a retrospective audit a significant time after the changeover of patients had happened and that in going through the records for various reasons which were not ascribable to failure of the change a lot of patients who had been switched were not included. The complainant said that what was being reported in the Glaxo audit appeared to be a subgroup of the total number who were originally changed to nizatidine. This brought into question the whole basis of the Glaxo audit data. Only very limited data had been made available in the public domain. The retrospective nature of the audit and the fact that it was reporting on a subgroup of the original number switched should have been made clear to the reader.

With regard to the claim "Uncertain cost savings" the complainant stated that the data concluded that cost savings would be likely from the success/failure rate given. The complainant queried the evidence against this as purely speculation without any basis. There was no indication that the detail aid was referring to anything other than drug costs. If other costs were being considered it should have been made clear. A changeover such as a therapeutic substitution might well increase workload in the initial period but many practices were prepared to accept this for accruing drug cost savings over months. The bullet points progressively built up an increasingly misleading message. The phrase "Solely to save costs" was loaded and disparaging implying unethical, unprofessional behaviour when in fact the motivation for the changes was ethical, the consideration of the cost effective use of NHS resources to maximise patient benefit. The claim "mainly because their symptoms were no longer under control" was misleading as it was stating as fact something which might or might not be the case and this could lead doctors to think that nizatidine was not as effective as ranitidine when there was no scientific basis for this and indeed the evidence did not support it.

RESPONSE FROM GLAXO

With regard to the claim "The pressure by Wirral FHSA to reduce Zantac prescribing has not reduced overall drug costs", the company submitted that the detail aid was produced in response to reports from general practitioners to sales representatives in the Wirral area that they felt under pressure to reduce Zantac prescribing by switching to cheaper H2 antagonists. The company understood that the pressure came from mailings and visits from local FHSA advisers. The complainant had visited general practitioners and said that Glaxo was incorrect in believing that general practitioners had been mailed by Wirral FHSA. The company had however seen examples of mailings from adjacent FHSAs urging doctors to switch from Zantac to cheaper H2 antagonists. The company acknowledged that the complainant might feel that her visits to general practitioners and discussions with them were merely advisory. It believed that many GPs perceived this as pressure to change prescribing especially as prescribing analysis and cost (PACT) data was used by FHSAs to monitor prescribing habits. The pressure to reduce Zantac prescribing was one of the reasons why the five practices were prepared to undertake an audit of the results of switching to nizatidine.

Glaxo provided a letter from a general practitioner in Wirral which stated that the vast majority of GPs had felt continued pressure overt or otherwise to reduce their prescribing costs. This pressure related to PACT statements, indicative budget statements, FHSA pharmaceutical representations, visits and reviews and more recently incentive methodology. The GP went on to say that the practice was offered a prescribing incentive if it reduced its drug costs by a specified amount. It was suggested that this could be achieved by changing ranitidine to nizatidine. The practice was not told to change but it was clearly in the practice's financial interests to initiate the change. The practice was encouraged to believe that there was little pharmaceutical difference between the products.

The detail aid was designed to be used in the Wirral area. Subsequently representatives from other areas became aware of it and requested copies. Since the company believed it to be factually correct it saw no reason why it was not valid for use outside the Wirral area or why the source of data should have been anonymised.

The graph headed "Wirral FHSA IMS Sterling sales" which appeared below the claim showed that overall acid suppressant drug costs were rising while Zantac sales were falling. Therefore the latter could not be contributing to these increasing costs. The company believed that whatever Wirral FHSA objectives were in encouraging a reduction in Zantac prescribing, it was factually correct to say that even when this was achieved overall drug costs were not reduced.

The complainant claimed that the objective was to slow down the rate of increase of prescribing costs for acid suppressants and provided confidential PACT data to support the argument that this had been achieved. As previously stated the item was based on BPI data which was in the public domain. This showed that whilst Wirral figures were generally comparable to the national picture the rate of growth based on the data source was generally higher than in other Mersey FHSAs.

With regard to the term "Uncertain cost savings" Glaxo said that the detail aid invited the reader to consider that the cost savings were uncertain. It was not as simple as changing from treatment A to cheaper treatment B to save £x. Apart from the costs of setting up the change, common sense and audit indicated that a proportion of patients would not, for whatever reason, be satisfied with the change. This incurred the additional and uncertain costs of futher visits, changed prescriptions, time off work and so on. The company did not see how the modest claim could be misleading. Glaxo was not clear whom the statement "Solely to save costs" could have disparaged since the general practitioners in the audit felt they were being asked to change patients' treatments merely to reduce their prescribing costs, which was after all what was measured by PACT data. In the case of switching from Zantac to nizatidine, it was difficult to see what direct benefit this offered patients since nizatidine was no more effective, it had a more limited range of indications and a safety record dervied from much smaller patient numbers.

With regard to the criticisms of the methodology used in the audit, the company had investigated further the doctor who had identified 64 patients that he had switched to nizatidine when only 22 had been included in the audit report by Penston *et al.* Dr Penston told Glaxo that the particular GP was asked to identify all the patients in his practice whose symptoms had been satisfactorily controlled while on long term ranitidine treatment who had been switched to nizatidine and followed up for several weeks following the switch. Dr Penston was informed by the GP that of the 64 patients, identified as switching to nizatidine only 22 fulfilled all the criteria. Dr Penston had examined the data on each of the patients in detail and found that the remainder of the 64 patients were excluded for one or more of the following reasons; they had never actually received nizatidine, there was no changeover - patients had received ranitidine at some time in the past but were not receiving ranitidine continuously in the weeks preceeding the start of nizatidine, no follow up data were available, one patient under went surgery and was unsuitable for follow up and one patient was on long term H2 antagonist therapy for prophylaxis during warfarin therapy and thus symptomless before and after changeover. The company rejected the criticisms of the audit results which it believed remained valid.

APPEAL BOARD RULING

The Appeal Board noted that the section of the detail aid referring to the audit was headed "Audit of five general practices in NW England".

The Appeal Board accepted Glaxo's submission regarding the audit. The Appeal Board considered that switching patients on any established therapy to another would cause problems for some patients as a number would always be dissatisfied with the change. The Appeal Board noted that the licensed indications for ranitidine and nizatidine were not the same. With regard to the phrase "Uncertain cost savings" the Appeal Board agreed with the Panel's view that there would be more costs associated with patients dissatisified with nizatidine than simply the cost of the replacement therapy. The costs of consulting the GP, wasted prescriptions etc should be taken into account when discussing savings. The Appeal Board considered that even in the absence of the audit data, the savings with the switch from Zantac to nizatidine were uncertain. The Appeal Board did not accept that the term was misleading and therefore ruled no breach of the Code. The appeal on this aspect failed.

With regard to the claim "The pressure by Wirral FHSA to reduce Zantac prescribing has not reduced overall costs", the Appeal Board considered that the claim was not misleading or disparaging as alleged. It considered that discussing prescribing in a therapeutic area with PACT data would be seen by general practitioners as pressure. This was not to say however that the FHSA had acted unreasonably. The Appeal Board accepted that a reduction in the overall drugs costs would not be expected. The Appeal Board ruled no breach of the Code. The appeal on this aspect failed.

With regard to the graph headed "Wirral FHSA IMS Sterling sales" the Appeal Board noted that the increase in sales in the acid suppressant market appeared to be a reasonably steady increase before the reduction in Zantac sales. The Appeal Board noted that the total acid suppressant market sales had continued this reasonably steady increase after the time that Zantac sales had started to decrease. The data shown were factual. The Appeal Board considered that readers would anticipate that the decrease in Zantac sales would slow the increase in the total acid supressant market sales and the graph showed that this did not appear to be so. There were of course a number of other factors which could have played a role such as increased interest from GPs in treating and increased prescribing of proton pump inhibitors. The Appeal Board considered that the graph was not unacceptable and therefore upheld the Panel's ruling of no breach of the Code. The appeal on this aspect failed.

The detail aid was withdrawn by 28 November 1995.

Complaint received **26 September 1995**

Case completed **17 January 1996**

CASE AUTH/342/10/95

STIEFEL v YAMANOUCHI

Bar chart in Dermamist brochure

Stiefel alleged that a bar chart in a Dermamist brochure issued by Yamanouchi was misleading in that data which was not statistically significant was used to imply that Dermamist was superior to Stiefel's product with regard to patient preference.

The Panel ruled that the bar chart was misleading as it conveyed the visual impression that there was a large difference between the products although this difference was not statistically significant.

COMPLAINT

Stiefel Laboratories (UK) Limited, a company not in membership of the ABPI, submitted a complaint about a brochure for Dermamist (ref YAM 56473) issued by Yamanouchi Pharma Ltd. The complaint concerned a bar chart headed "Patient preference Dermamist v bath emollient". The bars were labelled Dermamist 61% and bath emollient 39%. The information "n = 48 P = n.s" was also included. The complainant alleged that the bar chart was inaccurate as 61% of 48 patients was 29.28 patients and misleading in that it used data to imply superiority over Stiefel's product when the difference was clearly not of statistical significance. A breach of Clause 7.6 was alleged.

RESPONSE

Yamanouchi Pharma Ltd submitted that the bar chart gave a clear, fair and balanced view of matters relating to the subjective criterion of patient preference. The bar chart and the accompanying text made no reference to any specific product and therefore could not claim superiority over Stiefel's product. Yamanouchi pointed out that Stiefel stated that the difference was clearly not of statistical significance which in its opinion confirmed that the bar chart which stated "P = n.s" gave a truly balanced view of the matter.

Yamanouchi said that an unintentional error appeared in the bar chart in that the number of patients should be 46 and not 48 as stated in the brochure. This did not affect the heights of the bars or the percentages regarding patient preference. Having noticed the error, however, the company was reprinting the brochure and would be making the figures in the bar chart accurate to one decimal place. A copy of the proposed amendments was provided.

RULING

The Panel noted that it was a well established principle under the Code that non significant differences should not be presented in such a way as to give the visual impression of a substantial difference.

The Panel examined the bar chart and considered that readers would not necessarily know that the statement "P = n.s" meant that the difference was not statistically significant. The Panel noted that the figures for each bar were included on the bar chart but considered that, despite the labelling, the bar chart was misleading as it conveyed visually the impression that there was a large difference between the products as regards patient preference although this difference was not statistically significant. The Panel therefore ruled that the bar chart was misleading and in breach of Clause 7.6 of the Code.

Complaint received **4 October 1995**

Case completed **4 January 1996**

CASES AUTH/343/10/95, AUTH/344/10/95, AUTH/345/10/95, AUTH/346/10/95, AUTH347/10/95, AUTH/348/10/95, AUTH/349/10/95, AUTH/350/10/95, AUTH/351/10/95, AUTH/352/10/95, AUTH/353/10/95, AUTH/354/10/95, AUTH/355/10/95, AUTH/356/10/95 & AUTH/357/10/95

GENERAL PRACTITIONER v MEMBER COMPANIES & A NON MEMBER COMPANY

Sponsored articles in a journal

A general practitioner complained about a number of articles sponsored by pharmaceutical companies which appeared in a journal. The complainant alleged that the articles were purely advertising material and did not present an unbiased view. The conclusion reached on reading each article was that the best treatment was a drug produced by the sponsoring company. The identity of the sponsoring company was not made plain, although a small paragraph at the end of each article gave credit to the company for its educational grant.

The Panel decided that the articles, which were based on discussions by doctors, were not promotional as the companies concerned had had no direct editional input. The publishers had final editorial control. The sponsorship had been clearly declared as required. No breach of the Code was ruled.

COMPLAINT

A general practitioner alleged that the majority of an issue of a journal was in breach of the Code. Attention was drawn to fifteen articles sponsored by pharmaceutical companies. One of the sponsoring companies, although not a member of the ABPI, had nevertheless agreed to comply with the Code. The remainder were all member companies.

The complainant alleged that in every case the conclusion that could be reached on reading the article was that the best drug for the treatment of the conditions described was the drug produced by the sponsoring company. This was not made plain in the journal although in every case a small paragraph at the end of the article gave credit to the company for its educational grant.

The complainant stated that when he first received the journal he looked forward to reading it as a useful source of what he expected to be unbiased information. On closer scrutiny the conclusion reached was that it was purely advertising material and did not present an unbiased view. The reason for making the complaint was out of concern of it becoming more and more difficult to receive a reasoned article which could be of use.

RESPONSE

Each of the companies responded in detail about its involvement in the article it had sponsored. Given the nature of the matter, the publisher of the journal was also approached and provided details about the commissioning and production of the articles and the role of the sponsoring companies.

RULING

First, the Panel had to decide whether or not the articles were promotional items. The Panel noted that the whole area of company sponsored articles in publications, reports and symposia etc was not at all clear cut under the Code. Although the Authority received many enquiries, it had little in the way of precedent. A decision as to whether or not sponsored articles in a journal were promotional had to be taken on the facts of the particular matter. The Panel considered that the fact that a company had sponsored an article did not itself necessarily make that article promotional for the company's product.

The Panel noted that the sponsoring companies had very little involvement in the discussions upon which the articles in the journal were based. The companies had been able to recommend opinion leaders and provide a list of questions to be covered in the discussions. Final control had, however, remained with the publishers as to whom took part in the discussions and whether the suggested questions were even used.

The companies had not written the articles although they had seen them prior to publication for review. Some companies had made minor changes, mainly of an editorial/typographical nature. No substantial changes had been made. The Panel decided that the articles were not promotional as the companies had had no direct editorial input and the discussants and the publishers had final editorial control. It therefore followed that the material was not disguised promotion and no breach of Clause 10.1 was ruled. Similarly, as the articles were not promotional, prescribing information was not required with each article and the Panel therefore ruled no breach of Clause 4.1 of the Code. Finally, the Panel also ruled no breach of Clause 7.2 of the Code as the articles were not promotional.

With regard to the allegation that it was not sufficiently clear that the articles had been sponsored by particular pharmaceutical companies, the Panel noted that at the end of each article information was provided as to whom had sponsored the article. The inside cover of the journal stated that the managing editor was grateful to the sponsors. The inside back page of the journal listed by name all the pharmaceutical company sponsors.

The Panel noted that Clause 9.9 of the Code required that "All material relating to medicines and their use which is sponsored by a pharmaceutical company must clearly indicate that it has been sponsored by that company". The Panel considered that this clause required sponsorship to be clearly declared and this had been done. The Panel therefore ruled no breach of Clause 9.9 of the Code.

In the Panel's view however, it would have been more helpful if the sponsorship had been declared at the beginning of each article so that readers knew both that the article had been sponsored and by which company before reading it.

The Panel noted that its decision that the articles were non-promotional related to the fact that the articles had not been distributed by the pharmaceutical companies. If a pharmaceutical company were to request reprints of its sponsored article to be used for a promotional purpose, for example by representatives, then that would mean that all of the requirements of the Code would apply to the article including the requirement for prescribing information. The Panel requested that this be drawn to the attention of the sponsoring companies.

Complaint received 9 October 1995

Cases completed 5 January 1996

CASES AUTH/359/10/95 & AUTH/360/10/95

ASSISTANT PHARMACEUTICAL ADVISER WITH A HEALTH AUTHORITY v RHONE-POULENC RORER AND MERCK & LIPHA

"Dear Medical/Pharmaceutical Adviser" letter on Ikorel

An assistant pharmaceutical adviser complained about the promotion of Ikorel by Rhone-Poulenc Rorer Limited and Merck & Lipha Pharmaceuticals. There were three matters of complaint.

The Panel ruled that a claim "... effective monotherapy for up to 80% of patients" was misleading as the data ranged from 69% to 80%. This was overturned by the Appeal Board on appeal by the companies. The Appeal Board considered that as the range of data was narrow and the 80% figure was representative, the claim was not misleading.

The Panel did not accept an allegation that there had been a delay following the complainant's request for substantiation. Data had been sent promptly and follow up data had been sent within a month. The Panel therefore ruled no breach of the Code. This ruling was upheld by the Appeal Board on appeal from the complainant.

The Panel ruled that a cost comparison based on only the 10mg bd dose of Ikorel was misleading as it implied that the 10mg bd dosage was the most common dosage for therapeutic effect and this was not so. The data implied that the 20mg bd dosage would be the most common for therapeutic effect. This ruling was not appealed.

COMPLAINT

An assistant pharmaceutical adviser with a health authority complained about the promotion of Ikorel (nicorandil) by Rhone-Poulenc Rorer Limited and Merck & Lipha Pharmaceuticals. The material at issue was a "Dear Medical/Pharmaceutical Adviser" letter. The complainant sent copies of correspondence between herself and Rhone-Poulenc Rorer Limited.

It appeared from the correspondence that the complainant had telephoned Rhone-Poulenc Rorer and had left a message that she wished to see the source behind the claim "... effective monotherapy for up to 80% of patients" and that she was unhappy with the use of the 10mg bd dose as the basis for a cost comparison.

Rhone-Poulenc Rorer Limited had replied to the complainant. It stated that the claim relating to monotherapy was from a paper by Krumenacker and Roland and the quote in that paper referred to data on file. This data comprised the reports from three clinical studies which consisted of many hundreds of pages. The company was in the process of summarising the information and would send it to the complainant as soon as possible. In the meantime a paper by Wagner was sent which described a multicentered study in which 106 patients with stable chronic angina were enrolled. Of these patients 99 were eligible for efficacy evaluations. At six weeks and six months 87% and 81% respectively of patients were satisfactorily treated with 10 or 20mg nicorandil bd.

With regard to the cost comparison data, the company's view was that in general practice 10mg bd would be the most commonly used dose of Ikorel. This was borne out by the UK sales figures which showed a 7:1 ratio of sales of 10mg and 20mg tablets. These sales include hospital use in which a greater number of patients receiving 20mg bd might reasonably be expected.

The complainant's response to Rhone-Poulenc Rorer's letter (referred to above) formed the basis of the complaint.

The complainant said that it was unfortunate that the data on file was not available at the time Ikorel was launched and after 4 weeks she was still waiting for this information.

With regard to the effective dose, the complainant considered that the suggestion of a relationship between sales of Ikorel and the therapeutic dose used was clearly unrealistic. New medicines introduced into a hospital were nearly always purchased at the lowest strength and where increases in doses were necessary more than one tablet was taken. This would surely account for the 7:1 ratio of sales of 10mg to 20mg tablets. No hospital would purchase the 20mg tablets until the medicine had been shown worthy of being an addition to the formulary and stock could be guaranteed a usage.

The complainant said that the paper by Wagner stated that only 20% of the patients were controlled on 10mg bd of nicorandil. The other 80% required 20-40mg bd.

The complainant said that the more that she looked at the

product the less she was convinced by the data and hoped that the company would provide better information to support the claims being made for the product.

RESPONSE

Rhone-Poulenc Rorer responded on behalf of itself and Merck & Lipha. The mailing at issue had been sent to medical and pharmaceutical advisers as a one off item on Ikorel. The company provided a copy of the letter (ref RPR 4114 Merck & Lipha Code ZZ08054) and two leaflets (ref RPR 4111 and 4098 Merck & Lipha ZZ08044 and ZZ08044).

With regard to the alleged failure to provide substantiation of the claim "... effective monotherapy for up to 80% of patients", the company submitted that the original request was received by E Merck on 19 September 1995. The cited paper, Krumenacker and Roland, was sent by fax on 22 September and an original copy was posted the same day. Some further information which had been referred to in a telephone conversation about the product was forwarded on 26 September.

Subsequently the complainant contacted Rhone-Poulenc Rorer requesting unpublished data referenced by the authors of the Krumenacker and Roland paper. These data on file references were not cited in the mailing and had never been used directly in any promotional material for Ikorel. Some considerable work was required to retrieve and summarise the data. In a telephone conversation with the complainant on 26 September and in a subsequent letter dated 4 October, Rhone-Poulenc Rorer undertook to provide the summary of these unpublished references. In the meantime Rhone-Poulenc Rorer provided the complainant with the Wagner paper which showed that up to 87% of angina patients were controlled by monotherapy with nicorandil 10mg bd to 20mg bd. The summary was completed coincidentally with the arrival of the complainant's letter of 12 October and had now been sent to her. The reference cited in the mailing substantiating the claim was provided in a timely fashion in accordance with Clause 7.4 of the Code. In addition further information had been prepared and provided in an expeditious manner consequent upon discussions held between the complainant and the two companies.

Rhone-Poulenc Rorer submitted that the claim "... effective monotherapy for up to 80% of patients" was substantiated by the Krumenacker and Roland paper and the data on file references in the paper supported the claim. In addition the Wagner study also supported the claim.

With regard to the use of the 10mg bd dosage as the basis for a monthly cost, the company pointed out that the recommended starting dose for Ikorel, as stated in the data sheet, was 10mg bd although 5mg bd could be employed in some patients. The dose might be increased depending on the clinical response and the usual therapeutic dose range was 10mg bd to 20mg bd. The choice of 10mg bd was therefore consistent with the recommended licensed dose and the mailing clearly stated that the monthly cost indicated was for those patients requiring 10mg bd. As the company had pointed out there was good evidence of much more widespread use of the 10mg tablet compared to the 20mg tablet. The UK sales figures showed a 7:1 ratio for sales for the 10mg and 20mg tablets. This was further supported by prescription data. The cost information referred to an appropriate widely used dosage and clearly stated the formulation on which the cost was based. The company undertook not to use the claim "...but also a cost-effective one" until cost effectiveness studies became available.

PANEL RULING

The Panel noted that the claim "Ikorel is effective monotherapy for up to 80% of patients" was referenced to the Krumenacker and Roland review article, which stated in its summary that "Nicorandil is an effective and potent antianginal agent at a dose of 10-40mg which in monotherapy controls 69-80% of patients with stable chronic angina". A section in the paper under the heading "Long term efficacy" stated that at one year 69% of patients received nicorandil as monotherapy at a dose of 20mg bd. The Wagner paper also gave some support to the claim as at 12 months 80% of the patients were controlled on nicorandil as monotherapy. These patients received either 10mg bd or 20mg bd.

The Panel considered that it was misleading to claim that up to 80% of patients were controlled on monotherapy given that one paper showed that at 12 months 69% of patients were controlled on monotherapy. The claim as worded, although true, was not a reflection of all the evidence. The Panel considered that it was misleading to take a number of studies with different results and then report the results using the phrase "up to" and giving the maximum figure from the studies. The Panel therefore ruled a breach of Clause 7.2 of the Code.

With regard to the request for substantiation, the Panel noted that the claim in the letter was referenced to the Krumenacker and Roland review. The long term studies referred to in the review were referenced to data on file, Rhone-Poulenc Rorer. The Panel considered that as the Krumenacker and Roland paper was a review, it would have been helpful if the company had had the relevant data on file ready to send out if asked to do so. The company had sent the complainant the Wagner paper. The Panel did not consider that the delay in sending the data on file constituted a breach of the Code. Some data had been sent to support the claim. The Panel therefore ruled no breach of Clause 7.4 of the Code.

The Panel noted that the cost data appeared in the claim "The simple, twice-daily dosage for only £11.70 per month (in those requiring 10mg bd.) means Ikorel is not only an effective and convenient anti-anginal therapy but also a cost-effective one". The Panel examined the data and noted that almost all the efficacy data quoted in the Krumenacker paper was based on the 20mg bd dosage. The Wagner paper showed that 23% and 21% of patients were controlled on 10mg bd at 6 and 12 months respectively and 58% and 59% of patients were controlled on 20mg bd at 6 and 12 months respectively. The Panel also noted that the prescribing information stated that the normal therapeutic dose was 10 to 20 mg twice daily.

The Panel considered that the sales data was not meaningful in this discussion as sales of the 10mg tablet did not necessarily correlate with usage. The prescription data suggesting 10mg bd was the usual dose could not be used as support as there was no data to indicate that these

prescriptions resulted in effective treatment. In fact the study data suggested that this dose would not be effective in the majority of patients.

The Panel noted that the letter did include the dosage upon which the cost was based but considered that reference only to the 10mg bd dosage implied that this was the most common dosage for therapeutic effect and this was not so. The implication of the data was that the 20mg bd dosage would be the most common dosage for therapeutic effect. The Panel considered that the claim was misleading and therefore ruled a breach of Clause 7.2 of the Code. This ruling was accepted by the companies. The Panel noted that the company intended to cease making the claim as to cost effectiveness.

APPEAL BY COMPLAINANT

The complainant agreed that the Krumenacker and Roland paper was supplied promptly and this was used as a reference for the claim "...effective monotherapy in up to 80% of patients". The complainant pointed out, however, that the paper was a review which did not contain any satisfactory details of the relevant trials. The complainant was informed that the data was not available as it was being put on microfiche. The complainant requested clarification and was provided several weeks later with a study summary compiled from data on file. This information was far from useful, providing insufficient details of the study to make any assessment on effectiveness.

RESPONSE BY RHONE-POULENC RORER AND MERCK & LIPHA

The companies stated that the reference cited in the mailer, the Krumenacker and Roland paper, was provided to the complainant within 72 hours of the request. No data on file references were directly quoted in support of the claim. In addition following discussions with the complainant the summaries of the data on file references were prepared and were forwarded to the complainant on 17 October. The complainant had been provided with the Wagner paper on 4 October.

APPEAL BY RHONE-POULENC RORER AND MERCK & LIPHA

The companies pointed out that the Panel had agreed that the claim "Ikorel is effective monotherapy for up to 80% of patients" was true. By the use of the phrase "up to" the companies were clearly indicating that some studies had demonstrated efficacy in a smaller proportion of patients. The range of efficacy was between 69% and 80% of patients which the company submitted was a narrow range. The professionals for whom the literature was intended would know that data on the efficacy of a product would derive from several clinical studies all of which would show varying degrees of efficacy. This would vary according to the severity of the condition being treated, duration of therapy and the methods of assessment etc. The claim of "up to 80%" was used to convey a simple message for such heterogeneous data. The expression was widely used in peer reviewed medical and scientific journals to present the upper limit of a range of values. The company provided papers showing the use of the expressions in a range of highly reputable journals.

APPEAL BOARD RULING

The Appeal Board examined the data provided by the companies to support the claim that Ikorel was "...effective monotherapy for up to 80% of patients". It noted that the Krumenacker and Roland Review article to which the claim was referenced stated that at one year 69% of patients received nicorandil as monotherapy at a dose of 20mg bd. The Wagner paper also gave some support to the claim as at 12 months, 80% of patients were controlled on nicorandil as monotherapy (doses of 10mg bd or 20mg bd).

The Appeal Board accepted the companies' submission that the phrase "up to" was commonly used in peer reviewed journals to present the upper limit of a range of values. The Appeal Board considered that in order for the use of the phrase "up to" to be acceptable in promotional material the range of data must be narrow and the figure used to describe the limit of the range must be representive of all the data and not a rogue result.

The Appeal Board considered that in the circumstances the claim was not misleading and therefore ruled no breach of the Code. The appeal on this aspect therefore succeeded.

With regard to the complainant's appeal concerning the provision of data, the Appeal Board noted that the Krumenacker and Roland review article and the Wagner paper had been sent promptly to the complainant. The follow up data had been sent within a month of the original request. The Appeal Board considered that the requirement in Clause 7.4 of the Code that substantiation had to be provided without delay had been met. The Appeal Board therefore upheld the Panel's ruling of no breach of the Code. The appeal on this aspect therefore failed.

Complaint received **17 October 1995**

Case completed **17 January 1996**

CASE AUTH/361/10/95

GP v SCHERING-PLOUGH

Market research survey

A general practitioner complained about a market research survey about Schering-Plough representatives.

The Panel ruled that the survey was not disguised promotion and this was accepted by the complainant.

The Panel considered that the use of product names as brand logos on every page of the questionnaire meant that prescribing information was required. A breach of Clause 4.1 for the Code was ruled. This was appealed by Schering-Plough. The Appeal Board considered that the questionnaire was promotional and prescribing information was required. The Appeal Board therefore upheld the Panel's ruling. The Appeal Board's view was that it was inappropriate to include prescribing information on a market research questionnaire. Thus the questionnaire would have been undesirable even if it had included prescribing information. A genuine and non promotional market research exercise could, however, refer to the names of products in low key fashion without triggering the need for prescribing information.

COMPLAINT

A general practitioner complained about a questionnaire sent by Schering-Plough Ltd.

The questionnaire was a market research survey and asked questions about Schering-Plough representatives, Schering-Plough medical information department and Schering-Plough customer services. Printed on the bottom of each page of the questionnaire and the covering letter was the statement "We are talking about Schering-Plough Ltd whose products are..." followed by a list of the brand names (appearing as logos) Clarityn, DiproSalic, Rinstead, Drogenil, Elocon, DiproBase, Viraferon and Intron A.

The complainant queried whether the questionnaire was legal and said that he was concerned about the section in the questionnaire which asked recipients to rate Schering-Plough representatives compared to those of Astra and Glaxo Wellcome. The complainant was also concerned that the questionnaire appeared on paper which included brand names of Schering-Plough products.

RESPONSE

Schering-Plough submitted that it was clear from the questionnaire that no products were being promoted. The products were identified to ensure that the respondents were aware of which company was being assessed as many general practitioners and other audiences identified representatives with the products they promoted rather than the company they represented. In addition there was frequent confusion between Schering AG and Schering-Plough and displaying the product names seemed an obvious way of avoiding the confusion.

With regard to the comparison of Astra, Glaxo Wellcome and Schering-Plough representatives, the company submitted that the sole intention was to assess how its representatives compared with the two companies it regarded as the gold standard in the UK with a view to improving the services it offered and its image by identifying its own relative strengths and weaknesses.

PANEL RULING

The Panel noted that the questionnaire was in effect a market research questionnaire. The only requirement in the Code relating to market research was Clause 10.2 which stated that market research activities and the like must not be disguised promotion. The Panel considered that it was not unacceptable to compare the Schering-Plough representatives with those of Astra and Glaxo Wellcome. The Panel considered that the market research questionnaire was not disguised promotion and therefore ruled no breach of Clause 10.2 of the Code.

With regard to the inclusion of the product names on the paper, the Panel noted that the product names appeared as brand logos. Most of the products named were subject to the ABPI Code. The Panel noted that it was a long standing principle under the Code that the mention of a product name meant that prescribing information must be provided as required by Clause 4.1. The exceptions to this which were not relevant in this case were abbreviated advertisements (Clause 5) and promotional aids (Clause 18.3). Factual informative announcements and reference material relating for example to pack changes, adverse-reaction warnings, trade catalogues were also exempt from the Code (Clause 1.2). The Panel did not accept that the use of product names on the questionnaire was exempt from the requirement for prescribing information. The Panel therefore ruled a breach of Clause 4.1.

APPEAL BY SCHERING-PLOUGH

Schering-Plough was surprised that the Panel could conclude that prescribing information should have been provided. Surely had prescribing information been provided, the questionnaire would have been construed as disguised promotion.

The product names were included to avoid potential confusion with Schering AG and because representatives tended to be remembered more for their products than for their company. The company submitted that the inclusion of the product names was the most appropriate method of avoiding the confusion and obtaining accurate feedback.

Schering-Plough pointed out the consequence of the decision would be to make it impossible for any company abiding by the Code to conduct market research which mentioned any of its brand names. This would disallow vast proportions of the market research currently conducted by the UK pharmaceutical industry.

APPEAL BOARD RULING

The Appeal Board accepted that there was confusion between Schering-Plough and Schering Health Care.

The Appeal Board noted that the brand names appeared conspicuously as brand logos at the bottom of every page of the material, including the covering letter. There was no other reference to products as the questionnaire itself did not relate in any way to medicines or their usage. The Appeal Board accepted the submission that representatives tended to be remembered more for the products they promoted than for the companies they represented. It considered, however, that it would have been possible for the company to have given the brand names in the material in a low key fashion in the covering letter and this would have meant that prescribing information was not required. The problem was that the names were given conspicuously on each and every page as brand logos. The Appeal Board considered that the inclusion of the brand names on the questionnaire in this way meant that the material was promotional and prescribing information was thus required. The rest of the content was irrelevant to this decision. The Appeal Board accordingly upheld the Panel's ruling of a breach of Clause 4.1. The appeal therefore failed. Whether or not it was desirable for prescribing information to appear on a market research questionnaire was a separate matter.

The Appeal Board noted that the Panel had ruled that the material was not disguised promotion and that it needed prescribing information, which meant that the material had been regarded as promotion but not disguised promotion. This might be seen as somewhat confusing. The Appeal Board noted that the supplementary information to Clause 10.2 said that market research was "... the collection and analysis of information and must be unbiased and non promotional. The use to which the statistics or information was put may be promotional. The two phases must be kept distinct".

The only relevant provision in the Code, however, was the requirement that market research must not be disguised promotion. Other unsatisfactory features of market research which might be contrary to the Guidelines on Pharmaceutical Market Research Practice produced by the British Pharmaceutical Market Research Group (BPMRG) and the ABPI or to the Code of Conduct of the Market Research Society were not matters covered by the Code of Practice. The Appeal Board expressed the view, however, that it was inappropriate for market research and promotion to come together in the same document. Thus the questionnaire in the present case would have been undesirable even if it had included prescribing information. A genuine and non promotional market research exercise could, however, refer to the names of products in a low key fashion without triggering the need for prescribing information.

Complaint received **19 October 1995**

Case completed **21 February 1996**

CASE AUTH/362/10/95

UNIVERSITY DOCTORS/DIRECTOR v BAYER

Promotion of Ciproxin

A letter in The Lancet of 21 October 1995 critical of the promotion of ciprofloxacin (Ciproxin) by Bayer was taken up as a complaint under the Code.

The authors of the letter were critical of the use being made of data from Canada concerning reduced admissions for bronchitis and pyelonephritis in Quebec where the prescribing of ciprofloxacin was unrestricted as compared with Saskatchewan where its use was restricted. They considered that the evidence which had been made available was too brief to allow assessment of the methodology and that there were flaws in the analysis of the data.

The Panel considered that there was some evidence that ciprofloxacin reduced hospital admissions in asthmatic bronchitis and pyelonephritis. It considered that the use of the data in the promotional materials did not relect the limitations of the data. It was not made clear that the data referred to asthmatic bronchitis and not to bronchitis in general. The caveats of the originators of the data that the data were compatible with a hypothesis that ciprofloxacin was at least partly responsible for decreased hospitalisation rates had not been properly reflected in the promotional materials. The Panel ruled that the promotional materials were misleading.

COMPLAINT

A letter in The Lancet of 21 October 1995, which was critical of the promotion of ciprofloxacin (Ciproxin) by Bayer plc Pharmaceutical Division was taken up as a complaint under the Code in accordance with established procedure.

The authors of the letter said that Bayer had been distributing material promoting increased community prescribing of oral ciprofloxacin. Bayer's video and accompanying leaflet asserted that ciprofloxacin use in Quebec, where the drug was placed on the unrestricted formulary in 1989, might be responsible for reduced hospital admissions for bronchitis and pyelonephritis. No reduction was seen in Saskatchewan where the product's use was restricted. They were concerned about this marketing.

Firstly, the letter stated that the video was based on work published only in an abstract which was too brief to allow assessment of the methodology. Attempts to influence prescribing with the use of powerful and emotive media such as videos needed to be open to the rigours of independent analysis in keeping with Clause 7.2 of the Code.

Secondly, the letter stated that the analysis presented in the video seemed seriously flawed. Professor Le Lorier (one of the people conducting the study) had conceded

that a case control design was an inadequate basis for the claims he made. He had attempted justification by reporting no dependence of hospital admission rates on some possible confounders. He had attributed the total avoided hospital costs to ciprofloxacin and then concluded that use of ciprofloxacin was cost beneficial. The claims did not stand up to even superficial scrutiny.

The graph in the letter in The Lancet showed data taken from the video on which Professor Le Lorier's claims rested. It showed the calculated prevented hospital admissions for chronic bronchitis and the number of ciprofloxacin 750mg prescriptions for the four years up to March 1993. An important feature, not discussed on the video, was that the reduction in hospital admissions seemed to precede the uptake of ciprofloxacin, which was apparent as a sizeable intercept on the ordinate when the data was extrapolated linearly. A profoundly non-linear dependence of prevented hospital admissions on ciprofloxacin was possible but unlikely. A non-linear dependence would invalidate the health economic data used by Le Lorier, which was based on linear averages. There were other explanations for the intercept: errors in the calculations of avoided admissions, changes in coding practice; or any persistent structural change which coincided with the introduction of ciprofloxacin. The component of the reduction in admissions that had been noted to be associated with ciprofloxacin use was much lower than the total reduction in admissions. The authors of the letter calculated 24% for both types of infection.

The authors of the letter considered that these calculations undermined the argument that ciprofloxacin use was cost beneficial. On the basis of these figures the conclusion was reversed: ciprofloxacin use represented a net increase in expenditure on drugs and hospital admissions. The authors of the letter did not claim that their alternatives were necessarily correct but they did believe that a thorough examination of evidence that lay firmly in the public domain was needed before accepting Bayer's claims for ciprofloxacin.

RESPONSE

The promotional materials provided by Bayer were a video entitled "Ciproxin Le Lorier PEc - Canadian Study March 1995", a box of tissues with promotional material for Ciproxin (ref 9BCPT 766), a ring bound publication entitled "Go to work on infection" relating to Ciproxin, which appeared to be a detail aid, and a small folder entitled "Positive outcomes in the treatment of bronchitis. An audit of Ciproxin use in the community" which enclosed two leaflets, both with the title "A Positive Outcome" and with the subtitles "1: Avoiding hospitalisation costs" (ref 9BCPT 718) and "2: Reducing relapse rates" (ref 9BCPT 719) respectively. The latter item was understood to be a representatives' leavepiece.

Bayer said that although the video was developed for general practitioners and FHSA advisers, viewing in the hospital setting was not precluded for interested observers. The promotional materials could be received by doctors who did not see the video, as well as those who saw it.

Bayer believed that its use of Professor Le Lorier's data had been scrupulously fair and in no way misleading.

Bayer said that the study concerned was conducted by Professor J Le Lorier and Dr F Derdorian at the request of the Canadian Regional Health Board in an attempt to evaluate the overall clinical costs associated with drug use, and not merely those of drug acquisition. The only support provided by the company (Miles Inc, Canada) was funding the external statistical analysis of the data, at a time when the outcome of such an analysis was unknown. There was no Bayer/Miles input into this statistical analysis itself.

Bayer said that far from the statistical analysis being "seriously flawed" as alleged, the ARIMA (autoregressive integrated moving average) model was a well accepted statistical tool. Furthermore, the analyses were conducted twice: once by Professor Le Lorier himself and once by an independent statistician on a "blinded" basis. The raw data used by Le Lorier and information about the statistical methods used was provided.

Although the full paper relating to Professor Le Lorier's work had yet to be published, the findings and methodology had been presented in poster form at the Tenth International Conference on Pharmacoepidemiology (Stockholm, 1994) and subsequently published as an abstract. These were provided. The delay in the publication of the full paper (which was shortly to be submitted to "The Lancet") had been because of Professor Le Lorier's recent involvement with the Canadian Health Protection Board as there were perceived conflicts of interest while his involvement was continuing. To the company's knowledge, there had been no substantive criticism of the methodology employed prior to publication of the letter in The Lancet.

The methodological problems inherent in evaluating cause and effect in a study such as this were discussed in full by Professor Le Lorier himself on the video, in which he presented alternative hypotheses for the observed effects. Furthermore, in the leavepiece produced by the company it was stated that ciprofloxacin *may* have been responsible for the observed reduction in hospitalisation rate; and the conclusion of the piece was prefaced by a remark that an ecological correlation of this type "is a poor design to demonstrate causation". Nevertheless, all other factors examined suggested that there was indeed some linkage between increasing use of ciprofloxacin and reductions in hospital admissions in LRTIs and pyelonephritis.

Bayer said that the authors of the letter concentrated their criticism on the findings relating to admissions for chronic bronchitis and largely ignored the fact that a similar reduction in hospital admissions was also observed in pyelonephritis patients. Given that these were indications for which ciprofloxacin was most widely prescribed in Canada; that the observed findings did not correlate with the use of any other antibiotic; and that equivalent reductions in hospitalisation rate were not observed in other types of infectious disease, the study results strongly suggested that unrestricted ciprofloxacin prescription played at least some part in the findings. In this regard, if, as suggested in the letter, the observed effect may have been due to "errors in the calculations of avoided admissions", one would expect such errors to have been duplicated for other admissions as well but this was not the case.

Although Bayer did not claim that the total cash saving observed in Professor Le Lorier's study was necessarily entirely due to the unrestricted use of ciprofloxacin - there may indeed have been a pre existing downward trend in hospitalisation rates for the two conditions concerned - it did contend that the balance of evidence strongly supported the conclusion that ciprofloxacin usage patterns played a major part in the differences observed between the two Canadian provinces. Bayer believed that the evidence had not been presented in such a way as to mislead, nor had its significance been exaggerated.

Finally, Bayer believed that it had acted responsibly in focusing attention on the issue of total healthcare costs (and, by extension, patient well being and quality of life), rather than acquiescing in the over simplistic approach that restricted itself to drug acquisition costs alone. In that sense, while further work of this nature remained to be carried out, the Le Lorier abstract, and the publication that would shortly follow, provided an important "point of departure" for discussion of these wider issues within the medical community.

RULING

The Panel noted that Professor Le Lorier stated in the abstract that although an ecological correlation was a poor design to demonstrate causation, the time sequence, the strength of the association, the dose response, the biological plausability and the presence of a control population favoured an interpretation according to which ciprofloxacin was responsible for the decrease in hospitalisations for asthmatic bronchitis and pyelonephritis.

Further the Panel noted that Le Lorier's draft manuscript stated that "The least one could say is that these data are compatible with a hypothesis according to which the availability of ciprofloxacin is at least partly responsible for the decrease in hospitalisation rates for pyelonephritis and asthmatic bronchitis."

The Panel noted that the Le Lorier data referred to the treatment of asthmatic bronchitis (which the Panel understood was one type of bronchitis) and pyelonephritis. In the Panel's view, the conclusions of the study given in the abstract and the draft publication qualified the association of the use of Ciproxin and decreases in hospitalisation rates. Any promotional material should reflect this limitation.

The Panel examined each of the promotional materials in turn. The Panel noted that the transcript of the video referred to bronchitis and chronic bronchitis with no mention of asthmatic bronchitis. It did refer to the limitations of the data but clearly linked the decrease in hospitalisation rates to increased use of Ciproxin. None of the graphs included on the video were provided with the transcript. With regard to the box of tissues, the Panel noted that it included claims referenced to the Le Lorier study. On one side of the box the claim "Cost benefit with Ciproxin use in the community" and on another side the claim "Cost benefit in the community 24.6% reduction against projected hospitalisation rate per month in asthmatic bronchitis". A footnote on the box stated that this was "Data from a Canadian study which demonstrated the clinical and economic effect of unrestricted community prescribing of oral Ciproxin in Quebec compared to restricted community prescribing in Saskatchewan". The ring bound publication included similar claims to those on the box of tissues. The small folder included the claims "Effective community use can avoid hospitalisation costs" referenced to Le Lorier and "Cost benefit with Ciproxin use in the community" referenced to the Le Lorier study and to a study by Hoogkamp-Korstanje and Klein. Both claims appeared beneath headings "Positive outcomes in the treatment of bronchitis". Leaflet 1 referred to the audit of bronchitis and pyelonephritis and gave some detailed information about the study including stating that it related to asthmatic bronchitis and pyelonephritis hospitalisation rates. The leaflet also mentioned under the heading "Discussion Point" the caveats noted by the Panel. Leaflet 2 included the claim "Cost benefit with Ciproxin in the community" beneath the heading "Positive outcomes in the treatment of bronchitis" referenced to Le Lorier and Hoogkamp-Korstanje.

The Panel considered that there was some evidence that ciprofloxacin reduced hospitalisation rates in asthmatic bronchitis and pyelonephritis but the data were not being used in such a way as to reflect their limitations. In this regard, the Panel noted that the use of the data in the promotional material did not make it clear that the data referred only to asthmatic bronchitis and not to bronchitis in general. The authors' caveats regarding the study were reflected inadequately in Leaflet 1 and were not reflected at all in the other material. Use of claims such as "Cost benefit with Ciproxin use in the community" and "Cost benefit in the community 24.6% reduction against projected hospitalisation rate per month in asthmatic bronchitis" were making too much of the data. A breach of Clause 7.2 of the Code was ruled.

Case commenced **24 October 1995**

Case completed **16 January 1996**

CASE AUTH/364/10/95

PARKE-DAVIS v BOEHRINGER MANNHEIM

Bezalip Mono detail aid

Parke-Davis complained about a Bezalip Mono detail aid issued by Boehringer Mannheim. The Panel ruled that a page was misleading as it did not make it clear that the study described on the page was on another product, gemfibrozil, and not Bezalip Mono. The Panel also considered that the impression of the page was that Bezalip Mono was licensed for the primary prevention of coronary heart disease which was not so. The Panel therefore ruled that an unlicensed indication had been promoted. This was overturned by the Appeal Board on appeal by Boehringer Mannheim.

The use of a claim referring to a lower incidence of cardiac events was ruled by the Panel to be misleading as insufficient information had been given about the limitations of the study. The Panel also ruled a breach as the detail aid was more than 4 pages in length and did not include a reference as to where the prescribing information could be found.

Parke-Davis alleged a breach of Clause 2 of the Code as the detail aid discredited the industry. The Panel did not accept that the detail aid was such that it warranted a ruling of Clause 2 which was used as a sign of particular censure and reserved for such circumstances. The Appeal Board upheld the Panel's ruling on appeal by Parke-Davis.

Parke-Davis & Co Limited submitted a complaint about a Bezalip Mono detail aid used by Boehringer Mannheim UK (Pharmaceuticals) Limited. There were a number of allegations which were considered as follows:

1 Page headed "But the risk of CHD is multi-factorial"

COMPLAINT

Parke-Davis drew attention to a bar chart and statements appearing beneath it which were based on data from the Helsinki Heart Study. Both the graph and statements failed to state that the data was based on trial work using gemfibrozil (Lopid) and, by omitting this information and including a general reference to a fibric acid derivative, the page implied that bezafibrate (Bezalip Mono) was used in the Helsinki Heart Study. The page was alleged to be misleading in breach of Clause 7.2 of the Code. The ambiguous nature of the page would make it easy for a member of the medical profession to make incorrect assumptions about the clinical trial data supporting bezafibrate in the context of the Helsinki Heart Study.

Parke-Davis also alleged that the statement "The HHS primary prevention trial revealed" (which appeared immediately below the bar chart) implied that Bezalip Mono was licensed for the primary prevention of coronary heart disease (CHD). The presence of the brand name Bezalip Mono in large type at the bottom of the page strengthened the link between Bezalip and primary prevention. No information was provided to inform the reader that Bezalip was not licensed for primary or secondary prevention of CHD. In contrast, Lopid (gemfibrozil), the drug used in the Helsinki Heart Study, was licensed for the primary prevention of CHD.

RESPONSE

Boehringer Mannheim pointed out that Bezalip Mono was licensed for use in patients with fully defined and diagnosed hyperlipidaemias of Types IIa, IIb, III, IV or V, where diet alone was insufficient to correct the condition and where the risk associated with the condition warranted treatment. The main lipid fractions which were of differing clinical relevance according to the specific lipid abnormality within the licensed indications were total cholesterol, low density cholesterol (LDL-C), high density cholesterol (HDL-C), and triglycerides. The main drug groups currently used in the treatment of hyperlipidaemias in the UK were statins and fibrates. These drug groups had different effects on the individual lipid parameters. Statins were particularly effective in lowering total cholesterol and LDL-C. Fibrates were generally considered to be less potent than statins in lowering total cholesterol and LDL-C, but more effective than statins in increasing HDL-C and lowering triglycerides.

Boehringer Mannheim submitted that the detail aid showed that the context in which the Helsinki Heart Study data were used was to establish the clinical relevance of high triglycerides and low HDL-C levels. Page 1 indicated that the treatment of combined hyperlipidaemia involved more than lowering cholesterol levels. Page two outlined the demonstrated values of reducing cholesterol levels. Page three, the one in question, discussed other lipid fractions and this was clear from the heading "But the risk of CHD is multi-factorial." The Helsinki Heart Study data was used to show that high risk patients, those with a high LDL-C: HDL-C ratio (in other words low HDL-C levels) and hypertriglyceridaemia, were the patients who obtained greatest benefit in that study. The bar chart defined this sub group in that the two right hand bars were labelled LDL-C: HDL-C >5 + TG > 2.3mmol/l. The two bars on the left were the remainder of the study population supplying the base line risk of 1.00. The three stab points below the sub heading "The HHS primary prevention trial revealed" were simply repetitions of the visual information shown in the bar chart. The two stab points below the next sub-heading "In the high risk group" were a further breakdown of the lipid characteristics of this same high risk group.

Pages two and three (the page in question) had been used to establish that in treating combined hyperlipidaemia, the lipid fractions that were clinically important were high LDL-C, low HDL-C and high triglyceride levels. The next page dealt with the effects of bezafibrate on those three lipid parameters.

The page in question (page 3) was almost entirely devoted to the clinical outcome in the subgroup of patients to demonstrate that the risk of CHD was multifactorial and

to highlight that different groups have different risks.

Boehringer Mannheim had used the term "fibric acid derivative" to denote the class of drug used. No mention was made of any link between primary prevention of coronary heart disease and Benzalip Mono. The only use of the product name was at the foot of the page and the only claim relating to Bezalip Mono was the claim "Treating lipids with fibrinogen in mind".

PANEL RULING

The Panel examined the page in question and noted that it referred to the Helsinki Heart Study in some detail. No information had been provided regarding the fibrate used in Helsinki Heart Study, which was gemfibrozil, and this should have been stated. The Panel considered that in the absence of this information it would be assumed that the fibrate used was the advertised product, Bezalip Mono, and this was not so. The Panel noted that the brand name Bezalip Mono appeared at the bottom of the page. The Panel considered that the page was misleading and therefore ruled a breach of Clause 7.2 of the Code. This was accepted by Boehringer Mannheim.

The Panel also considered that the claim "The HHS primary prevention trial revealed" on the page gave the impression that Bezalip Mono was licensed for the primary prevention of coronary heart disease and this was not so. No information was provided to inform the reader that Bezalip Mono was not licensed for the primary or secondary prevention of coronary heart disease. The Panel noted that the complainant had alleged a breach of Clause 7.2 with regard to this aspect of the complaint. The Panel decided, however, that the more appropriate clause was 3.2 which prohibited the promotion of an unlicensed indication. The Panel therefore ruled a breach of Clause 3.2 of the Code. This was appealed by Boehringer Mannheim.

APPEAL BY BOEHRINGER MANNHEIM

Boehringer Mannheim submitted that the sub-heading "The HHS primary prevention trial revealed was not a claim but a factual statement which was followed by three stab points which were repetitions of the visual information shown in the bar chart. The two stab points which appeared under the sub heading "In the high risk group" were a further breakdown of the lipid characteristics in this same high risk group. The context in which the Helsinki Heart Study data was used was to establish the clinical relevance of high triglycerides and low HDL-C levels precisely in line with the authors' conclusions. The only reference to Bezalip Mono on the page was at the foot of a page. The product name and accompanying strapline "Treating lipids with fibrinogen in mind" appeared at the foot of each right hand page of the detail aid. This was a stylistic feature of the piece and not an attempt to link the product with the Helsinki Heart Study data. This statement was the only product claim which appeared on page three and established that Bezalip Mono was a lipid altering drug and could not be construed to infer that the product was licensed for use in the primary prevention of coronary heart disease.

The Bezalip Mono data sheet stated that "Bezalip should be employed only in patients with a fully defined and diagnosed lipid abnormality which is inadequately controlled by dietary means, or by other changes in life-style such as physical exercise and weight reduction, and in whom the long-term risks associated with the condition warrant treatment". The data sheet went on to say that "The rationale for the use of Bezalip Mono is to control abnormalities of serum lipids and lipoproteins to reduce or prevent the long term adverse effects which have been shown by many epidemiological studies to be positively and strongly correlated with such hyperlipidaemias". The company submitted that Bezalip Mono was licensed for the reduction or prevention of long term adverse effects associated with hyperlipidaemas.

APPEAL BOARD RULING

The Appeal Board noted that the detail aid was used with a specialist audience being selected senior hospital doctors with a known interest in hyperlipidaemas. It accepted that the page in question was setting out an argument relating to raised lipid levels and coronary heart disease. The Appeal Board noted that the data sheet for Bezalip Mono stated "The rationale for the use of Bezalip Mono is to control abnormalilties of serum lipids and lipoproteins to reduce or prevent the long term adverse effects which have been shown by many epidemiological studies to be positively and strongly correlated with such hyperlipidaemias". The Appeal Board accepted the submission from the company. The page was not unreasonable given the statement in the data sheet noted above. The Appeal Board ruled no breach of Clause 3.2 of the Code. The appeal on this point was therefore successful.

2 Statement "High-risk patients treated with a fibric acid derivative (FAD) had a 71% lower incidence of cardiac events by comparison"

COMPLAINT

Parke-Davis reminded the Authority that in a previous case (Case AUTH/24/3/93) the Panel had found Parke-Davis in breach of the Code concerning the use of data derived from the post hoc analysis of high risk individuals in the Helsinki Heart Study featured in promotional material for Lopid.

Parke-Davis alleged that the statement in the Bezalip Mono detail aid that "High-risk patients treated with a fibric acid derivative (FAD) had a 71% lower incidence of cardiac events by comparison" was in breach of Clauses 7.2 and 7.8 of the Code as the data had been considered to be exaggerated and all embracing in the Panel's ruling in Case AUTH/24/3/93. The statement in the Bezalip Mono detail aid had not been sufficiently qualified in that it failed to reflect the sub study to which it was referenced. The authors of the study stated that "caution is also necessary in the interpretation of these findings as they are based on a post-hoc analysis of subgroups not defined in the original study plan" and "It is important to note that our conclusions are based on a cohort of initially healthy hyperlipidaemic middle-aged men and are not necessarily generalizable to other populations". As well as this, the detail aid did not qualify the statement by indicating that it referred to a subgroup of men aged 40-55 years of age with LDL/HDL >5 and triglycerides

>2.3mmol/l who had not responded to diet (154 patients out of 23,000). However, the Panel had considered the claim for a 71% reduction to be misleading even with these qualifications.

RESPONSE

Boehringer Mannheim submitted that the Panel's consideration of the Case AUTH/24/3/93, and the basis of its finding, was not applicable. In this regard, the company pointed out that the authors'statement "it is important to note etc" was not referring to the sub-analysis but to the entire study. The reference to Lopid only being indicated in men aged 40-55 years of age was not relevant to Bezalip Mono which had no such restriction in its licence.

Boehringer Mannheim submitted that it made no claim directly or by implication that Bezalip Mono reduced coronary heart disease by 72%. The statement "high-risk patients treated with a fibric acid derivative (FAD) had a 71% lower incidence of cardiac events by comparison" was appropriate and consistent with the study data.

PANEL RULING

The Panel considered that the page in the detail aid did not give sufficient information about the limitations of the study in that the authors of the study had stated "Caution is also necessary in the interpretation of these findings, as they are based on a post hoc analysis of subgroups not defined in the original study plan. It is important to note that our conclusions are based on a cohort of initially healthy, hyperlipidaemic middle-aged men and are not necessarily generalizable to other populations".

The Panel considered that the use of the claim was misleading and therefore ruled a breach of Clause 7.2 of the Code. This was accepted by Boehringer Mannheim.

3 Reference to prescribing information

COMPLAINT

Parke-Davis alleged a breach of Clause 4.6 of the Code as no reference to where the prescribing information could be found was included on the outer edge of the initial page in at least 8 point type.

RESPONSE

Boehringer Mannheim said that Clause 4.6 did not impose the obligations referred to by Parke Davis, therefore the obligations had not been breached.

PANEL RULING

The Panel noted that Clause 4.6 required that in the case of printed promotional material consisting of more than four pages, a clear reference must be given to where the prescribing information could be found. The detail aid in question consisted of eight pages and there was no reference as to where the prescribing information could be found. The Panel therefore ruled a breach of Clause 4.6 of the Code. This was accepted by Boehringer Mannheim.

4 Alleged breach of Clause 2

COMPLAINT

Parke-Davis alleged that the misleading claims and data used clearly discredited the good name of the pharmaceutical industry. The detail aid was an obvious attempt to mislead medical practitioners both by omission and by reference to important landmark trials such as the Helsinki Heart Study and 4S, which did not use bezafibrate in their design. A breach of Clause 2 of the Code was alleged.

RESPONSE

Boehringer Mannheim submitted that the detail neither misled nor brought discredit upon the industry.

PANEL RULING

The Panel did not consider that it was unacceptable in principle to use data from studies not carried out on the product being promoted provided that it was not presented in a misleading way as had been done with the data from the Helsinki Heart Study which the Panel had ruled in breach of Clause 7.2 of the Code. The detail aid had made it clear that the 4S study was on simvastatin which had been named as the product under investigation. This appeared on page 2 of the detail aid where there was no mention of Bezalip Mono by either brand or generic name.

The Panel did not accept that the detail aid was such that it warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and was reserved for such circumstances. The Panel therefore ruled no breach of Clause 2 of the Code. This was appealed by Parke-Davis.

APPEAL BY PARKE-DAVIS

Parke-Davis said that Boehringer Mannheim's use of the Helsinki Heart Study to promote Bezalip in a wholly misleading way to the medical profession was a gross breach of the Code. Moreover intentional acts of this kind should not be tolerated and such activity should be dealt with in a firm way to deter future activities. Action must be taken to prevent this kind of intentional misinformation of the medical profession with the sole aim of meeting marketing objectives.

Parke-Davis said that simvastatin was mentioned specifically in the detail aid in connection with the 4S study, gemfibrozil was not mentioned as the trial drug in the Helsinki Heart Study. The detail aid referred only to a fibric acid derivative as the trial drug which directly implied that bezafibrate was used as a large logo displaying Bezalip appeared underneath statements referring to the study. In no part of the detail was gemfibrozil mentioned by name. Indeed the very fact that the company used two different approaches in the same promotional piece, once to correctly acknowledge simvastatin but then to plagiarise Lopid's results from the Helsinki Heart Study was evidence of calculated, premeditated nature of the deception.

RESPONSE BY BOEHRINGER MANNHEIM

Boehringer Mannheim submitted that Bezalip Mono was promoted to hospital physicians with a known interest. The Helsinki Heart Study was very well known to the audience as a landmark study and it was widely known amongst the audience that gemfibrozil was used. Any attempt to deliberately mislead these specialists would render the company a laughing stock, devoid of credibility.

The company had not received any questions or comments from doctors on whether Bezlip Mono was used in the Helsinki Heart Study.

The product name was not directly under the Helsinki Heart Study data, but was separated from it by four lines of text relating to recommendations of the European Atherosclerosis Society, clearly referenced from a different source to the Helsinki Heart Study. Furthermore immediately under the brand name was the statement "Treating lipids with fibrinogen in mind" which established Bezalip Mono as a lipid altering product.

APPEAL BOARD RULING

The Appeal Board noted that Boehringer Mannheim had accepted a number of breaches of the Code in relation to the detail aid. The Appeal Board did not consider that the detail aid was such that it warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such circumstances. The Appeal Board therefore upheld the Panel's ruling that there was no breach of Clause 2 of the Code. The appeal on this point therefore failed.

Complaint received **23 October 1995**

Case completed **28 February 1996**

CASE AUTH/366/10/95

PHARMACIST WITH AN NHS BODY v ROCHE

Journal advertisement for Rocephin

A pharmacist with an NHS body complained that a claim "The world's best selling injectable antibiotic" in an advertisement for Rocephin issued by Roche Products Limited was misleading. It was alleged that the claim might mislead prescribers into believing that Rocephin was the most popular or most widely prescribed injectable antibiotic.

The Panel considered that the claim was misleading as it did not make it sufficiently clear as to what was meant by the term "best selling". It noted that the company's use of the term related to the value of the market whereas in the Panel's view the term would be taken to mean that the product sold more doses than any other injectable and not that it was the leader in total cash sales. A breach of the Code was ruled.

COMPLAINT

A pharmacist with an NHS body drew attention to a claim "The world's best selling injectable antibiotic" which had been appearing in journal advertisements for Rocephin issued by Roche Products Limited. The complainant referred to an advertisement in The Lancet, 21 October 1995, in which this claim was the main heading.

The complainant pointed out that there was a reference quoted to support the claim and this appeared to indicate that that claim was based on estimated current cash sales worldwide. The complainant pointed out that those in the business of marketing pharmaceuticals might understand the term "best selling" in terms of absolute amounts of cash revenues generated by the sale of a product but to a health professional the term "best selling" might convey the idea that the product was the most widely prescribed antibiotic, in other words the one which sold in the largest quantities.

The complainant accepted that the reference indicated that the claim related to the estimated cash sales but considered that it was not sufficient to explain what was meant by the term "best selling". The claim was alleged to be misleading as suggesting that Rocephin was the best selling injectable antibiotic might mislead prescribers into believing that it was the most popular or most widely prescribed.

RESPONSE

Roche provided information from Intercontinental Medical Statistics (IMS) to confirm Rocephin's position as the world's best selling injectable antibiotic. The company also included a table published in PharmaBusiness July/August 1995. Both of these substantiated the claim as being accurate and based on up to date data.

The company submitted that in the Shorter Oxford Dictionary each of the definitions for the word "sell" included a reference to "money" or "something that was reckoned as money" and therefore the term "best selling" must clearly relate to cash value and not to any other measure.

The company pointed out that on each of the advertisements which carried the claim, it was referenced as "Data on file Roche Products Limited", and in the reference section it was also made abundantly clear that the company was referring to "estimated current cash annual sales worldwide". If the company had data to support the claims "most widely prescribed" or "most popular" then it would have made and referenced those claims.

RULING

The Panel noted that the IMS data supplied by Roche stated that Rocephin was the clear leader in sales of injectable antibiotics for the 12 months ended December

1994. The table in PharmaBusiness included worldwide sales levels of Rocephin.

The Panel noted that the company's use of the term "best selling" related to the value of the Rocephin market and was not related to the number of doses sold. It would be possible for an expensive medicine to sell a small number of doses and still have the largest sales in cash terms whereas a cheaper product might sell more doses but, as each cost less, the product might have lower total sales in cash terms.

The Panel considered that when the term "best seller" was used in relation to books, for example, it would be taken by the general public to mean a book which sold a large number of copies rather than a book with large sales in cash terms.

The Panel considered that readers of the advertisement would interpret the claim "the world's best selling injectable antibiotic" as meaning that Rocephin sold more doses than any other injectable and not that Rocephin was the leader in total cash sales, as was in fact the position.

The Panel considered that the claim was misleading as the claim itself did not make it sufficiently clear as to what was meant by the term "best selling". The Panel therefore ruled a breach of Clause 7.2 of the Code.

The Panel noted the submission from the company that the claim was referenced and that it was clear that it referred to estimated current cash annual sales worldwide. The Panel did not accept this as no reference was given where the claim appeared as a main headline and, in any event, it was an established principle under the Code that one could not make a misleading claim and qualify it in small print elsewhere within the text.

Complaint received **25 October 1995**

Case completed **10 January 1996**

CASES AUTH/367/10/95 & AUTH/373/11/95

PHARMACEUTICAL ADVISER TO FAMILY HEALTH SERVICES AUTHORITY & JANSSEN-CILAG v SCHERING

"Dear Colleague" letter on oral contraceptives

A pharmaceutical adviser to a family health services authority and Janssen-Cilag complained alleged that a "Dear Colleague" letter sent by Schering Health Care was misleading. The letter referred to the Committee on Safety of Medicines (CSM) advice regarding oral contraceptives.

The Panel ruled that the letter was misleading as it gave the impression that the CSM advice was that women on the preparations at issue should be switched to a suitable levonorgestrel preparation, a number of which were made by Schering. This was not in accordance with the CSM advice as acknowledged by Schering.

The Panel ruled no breach of the Code with regard to Janssen-Cilag's allegation that the letter was in breach of Clause 2 of the Code.

Case AUTH/367/10/95

COMPLAINT

A pharmaceutical adviser to a family health services authority, complained about a "Dear Colleague" letter sent by Schering Health Care Limited. The complainant alleged that a paragraph in the letter was inappropriate.

The paragraph at issue was as follows:

> "The CSM advice is that users of these preparations, which currently account for about 50% of the UK market, should be switched at the end of the current course of those pills to a suitable levonorgestrel preparation. A number are manufactured by Schering which include Microgynon 30, Logynon and Eugynon 30. Should individual patients wish to switch immediately then instructions are enclosed to facilitate this".

The complainant stated that her interpretation of the Committee on Safety of Medicines (CSM) advice was that desogestrel and gestodene were associated with a two fold increase in thromboembolism compared with levonorgestrel, norethisterone or ethynodiol. It was not known if norgestimate was associated with an increased risk because of insufficient evidence at present. Oral contraceptives containing desogestrel and gestodene should be reserved for women who were intolerant of other oral contraceptives and those who were prepared to accept an increased risk of thromboembolism. They should not be used in women who were obese, who had varicose veins or a previous history of thrombosis from any cause.

The complainant stated that the CSM had not made any specific recommendations regarding products which were considered to be suitable. The complainant alleged that the letter was misleading and incorrect.

RESPONSE

Schering Health Care advised that the letter was sent to general practitioners, practice managers, practice nurses, retail and regional and drug information pharmacists, wholesalers, public health directors, health authority chief executives and medical and pharmaceutical advisers.

The company acknowledged that a mistake was made in the "Dear Colleague" letter. The CSM advice was of course not to switch to a suitable levonorgestrel pill although in the "Dear Doctor/Pharmacist" letter from Professor Rawlins of 18 October 1995, levonorgestrel was among the progestrogens for which the "investigations provide reassurance" about associated thromboembolic risks.

The company accepted that the letter was a technical

breach of the Code but did not believe that it contravened the spirit of the Code. At the time of writing the letter, the company was very much aware of the paramount need for speed in issuing helpful information to doctors and patients. It felt that it was best placed to offer advice on its own levonorgestrel containing products as it was familiar with them and was in a position to guarantee continuing supply so that patient needs could be met. With the late inclusion of a phrase from its parent company, it failed to observe the way the meaning of the sentence was changed. In its haste the error occurred and was missed on subsequent scrutiny.

The company was surprised by the suddenness of the CSM advice and was unable to act with its usual high degree of caution and consideration when events compelled it to send the "Dear Colleague" letter. The letter was not intended to be a promotional piece but was meant to offer helpful technical advice to prescribers.

The company had attempted to clarify the issue with the recipients by a second letter which referred recipients to the original CSM letter rather than to its summary.

RULING

The Panel considered that the paragraph in the "Dear Colleague" letter referring to advice from the CSM was misleading as it gave it the impression that the advice was that women on the preparations at issue should be switched to a suitable levonorgestrol preparation. This was not in accordance with the CSM advice as acknowledged by the company. The Panel therefore ruled a breach of Clause 7.2 of the Code.

Case AUTH/373/11/95

COMPLAINT

Janssen-Cilag alleged that the letter sent by Schering Health Care falsely represented the CSM advice by stating "The CSM's advice is that users of these preparations...should be switched at the end of the current course of these pills to a suitable levonorgestrel preparation". Janssen-Cilag had contacted Schering seeking an immediate rectification of this falsehood but to no avail. Given the seriousness of this misrepresentation of the CSM advice and a need for urgent correction the company had informed the Medicines Control Agency. Breaches of Clause 7.2 and Clause 2 of the Code were alleged.

RULING

The Panel decided that the allegation in this case was similar to that already considered in Case AUTH/367/10/95 in which the Panel had ruled that the paragraph in the "Dear Colleague" letter referring to advice from the CSM was misleading in breach of Clause 7.2 of the Code. The Panel decided that its ruling of a breach of Clause 7.2 also applied in this case.

With regard to the alleged breach of Clause 2 of the Code, the Panel did not accept that the material was such that it warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and was reserved for such circumstances. The Panel therefore ruled no breach of Clause 2 of the Code.

Case AUTH/367/10/95	
Complaint received	**27 October 1995**
Case completed	**11 December 1995**
Case AUTH/373/11/95	
Complaint received	**17 November 1995**
Case completed	**13 December 1995**

CASE AUTH/368/10/95

NATIONAL PHARMACEUTICAL ASSOCIATION v ROCHE

Malaria advice leaflet for patients

The National Pharmaceutical Association complained that the phrase "... don't "pop round to the chemist" you risk taking the wrong tablets and that could be fatal" which appeared in a malaria advice leaflet for patients issued by Roche was offensive and an slur on the profession.

The Panel ruled that the phrase was in breach of the Code as it disparaged pharmacists as a profession and thereby failed to recognise the special nature of medicines and was not in good taste.

COMPLAINT

The National Pharmaceutical Association (NPA) complained about a leaflet headed "Essential advice about malaria for British travellers to tropical countries" (P468066 6/95). The NPA pointed out that it was not apparent from the text in the leaflet that it had been produced by Roche Products Limited. This information was given on the display unit. The NPA drew attention to a paragraph headed "Take protective medicines" which included the wording "... don't "pop round to the chemist". You risk taking the wrong tablets - and that could be fatal". The NPA alleged that the wording was offensive and a slur on the pharmaceutical profession. The leaflet was considered by the NPA Board of Management which was outraged at the wording used in the leaflet and it had instructed the Deputy Director of the NPA to lodge a complaint with the Authority in addition to expressing its objections direct to Roche.

RESPONSE

Roche Products Limited said that the leaflet in question had already been withdrawn following a previous case,

Case AUTH/334/9/95, when the Panel had ruled the leaflet to be inaccurate in breach of Clause 20.2 of the Code. Roche said that it had informed the NPA that the leaflet had been withdrawn and apologised unreservedly for any unintentional offence caused.

The company appreciated the NPA's distress and was contacting it directly to make the position clear.

Roche stated that in view of the fact that the leaflet had been ruled in breach previously and in light of the foregoing it assumed that no further action would follow.

The Authority advised Roche that the matter would need to be considered by the Code of Practice Panel in accordance with the Constitution and Procedure.

RULING

The Panel noted the requirements of Clause 9.1 of the Code that all promotion must recognise both the special nature of medicines and the professional standing of the audience to which it is directed and that good taste must be observed in respect of the illustrations, text and themes of promotional material and activities. The Panel considered that the use of the phrase "don't pop round to the chemist", disparaged pharmacists as a profession and thereby failed to recognise the special nature of medicines and was not in good taste. The Panel therefore ruled a breach of Clause 9.1 of the Code.

Following the Panel's consideration, the NPA requested that the complaint be withdrawn as it had received an apology from Roche and an apology had appeared in The Pharmaceutical Journal.

It was not possible for the complaint to be withdrawn at the Constitution and Procedure only allowed complaints to be withdrawn with the consent of the respondent up until such a time as the respondents comments had been received.

Complaint received **31 October 1995**

Case completed **13 December 1995**

CASE AUTH/369/11/95

DOCTOR v ORGANON

Letter concerning Marvelon and Mercilon

A consultant in pharmaceutical medicine complained about a "Dear Doctor" letter sent out by Organon. The letter was about advice issued by the Committee on Safety of Medicines (CSM) in relation to combined oral contraceptives and it referred to Organon's products, Marvelon and Mercilon.

It was alleged that the letter was promotional in nature, that it should therefore have complied with the Code and that it was critical of the CSM. Such criticism was unwarranted and brought the industry into disrepute.

The Panel considered that the letter was promotional in nature and that it was in breach of the Code because it had failed to include prescribing information. The Panel considered that the letter had not disparaged the CSM and had not brought the industry into disrepute. The rulings were upheld by the Appeal Board upon appeal by the complainant.

COMPLAINT

A consultant in pharmaceutical medicine complained about a "Dear Doctor" letter which had been sent to doctors by Organon Laboratories Ltd. The letter was about recent advice issued by the Committee on Safety of Medicines (CSM) in relation to combined oral contraceptives and referred to the Organon products, Marvelon and Mercilon.

The complainant said that the statement by the company "We remain confident in our products and their risk-benefit profile ...." made the letter promotional and it should therefore comply with Clauses 4.2 and 7.3 of the Code. The complainant was particularly concerned about the criticism of the CSM in that it "....acted hastily in issuing advice to doctors on unpublished, unreviewed and incomplete studies". Data submitted to the Medicines Control Agency (MCA) to obtain a product licence invariably contained material produced by the manufacturer which was confidential and unpublished. The complainant had never heard of anyone complaining that the CSM should fail to consider it because it had not been reviewed and/or published.

The complainant considered this criticism by Organon to be unwarranted and that it brought discredit upon the pharmaceutical industry.

The Authority drew Organon's attention also to Clauses 2 and 8.2 of the Code.

RESPONSE

Organon said that in order to respond comprehensively to the complaint, it was necessary to provide some background information. There were many remarkable aspects surrounding the current controversy on oral contraceptives.

1 Timings

The timescale of events as they occurred was:

- 11 October — UK Authorities met with investigators of three epidemiological studies.
- 12 October — Companies attended meeting with MCA.
- 13 October — Special CSM meeting, excluding company representatives, held to discuss findings.
- 16 October — Ministerial decision taken to authorise the CSM decision.
- 18 October — (11am - 2pm) Committee on Proprietary

	Medicinal Products (CPMP) meeting. Investigators presented their findings.
•18 October	CSM Dear Doctor letter posted.
•18 October	(8.30pm) Faxed copy of CSM Dear Doctor letter received by Organon.
•19 October	CSM Press release sent to Organon by the BBC Newsroom.
•26/27 October	CPMP Special meeting.
•27 October	CPMP Press release.
•28 October	British Medical Journal (BMJ) articles.
•1/2 November	Dear Doctor letter from Organon (the subject of complaint).

As could be seen from this summary, events had occurred very rapidly indeed, with only one week elapsing between the presentation by the investigators and the posting of a letter by the CSM. It should be noted that the letter was posted on the day that the data in question were presented to the CPMP, before a CPMP opinion was reached and in spite of a CPMP request to national authorities not to take hasty action. It was also clear that the three companies involved, Organon, Schering and Wyeth, had only a few hours warning before a decision was taken by the CSM. They had no opportunity of a hearing before the CSM or the CPMP, nor indeed time to prepare for such a hearing.

2 Confusion to doctors and to the public

There were several unique factors to the situation as it unfolded which Organon thought should be highlighted.

- Never before had there been a pharmacovigilance issue which had affected so many patients.
- Never before had a decision of this importance been based on preliminary data
- Never before had the publicity been so badly handled.
- Never before had the credibility of the CSM been undermined in the eyes of the medical practitioners, patients and the pharmaceutical industry.

In the week immediately after the CSM letter, Organon (and the other companies involved) received countless calls from doctors and women who were confused by the conflicting advice offered by the CSM. The Food & Drugs Administration (FDA) in the USA, the MCA and the BBC (which had set up hotlines) also received many thousands of calls. Problems were caused since patients had heard about the scare through the media and were contacting their doctors for advice before the doctors had received the CSM letter. This put doctors in a very awkward position as patients were demanding information on a situation that they knew nothing about. As the farce unfolded, doctors were still not given access to the data on which the CSM decision had been made, making it extremely difficult for them to give accurate, informed advice to women seeking reassurance. The only basis which doctors had for giving advice was the CSM letter which was itself contradictory. Articles in the BMJ questioned not only the CSM's action, and the speed at which it was taken, but also why the CSM had proceeded on the basis of preliminary data which had yet to be completely analysed and caused further confusion.

A week after the CSM letter, the CPMP reached an opinion which conflicted with the advice given by the CSM. The CPMP press release stated that it "did not consider it appropriate to withdraw combined oral contraceptives containing gestodene or desogestrel" (Marvelon and Mercilon contain desogestrel) and that it would review the situation within 6 months, once further data had been made available by the investigators and the companies involved. This statement thus introduced another contrasting position into the mess from which doctors were supposed to retrieve accurate advice for their patients. The CPMP had UK representatives among its members.

The CSM had not sought to clarify the situation since the CPMP press release and had not commented on the position taken by the CPMP. Nor had it provided further information to doctors. Furthermore, the legal status of the CSM letter following the CPMP opinion and press release was open to question. It was apparent that the CPMP statement superseded that of the CSM, thus explaining the total lack of communication or action from the CSM since its letter was published.

3 Current UK regulatory situation

The CSM letter had so far not led to any regulatory action by the MCA on the marketing authorizations for Marvelon or Mercilon. Since there was uncertainty over the legality of the CSM letter, and its relevance in light of the subsequent CPMP opinion, Organon could only note that the actual legal situation was that its marketing authorizations had not changed. Therefore Organon felt fully entitled to defend the terms of those marketing authorizations.

4 Consensus of medical opinion

The current confusion, as described above, had made it difficult to see where the consensus of medical opinion lay. However it was notable that there had been no support for the CSM from any person who had seen the preliminary results of the epidemiological studies in question. (The German regulatory authorities had proposed to take action on the oral contraceptives in question, but not the same action as the CSM). In fact there seemed to be a considerable sway away from the CSM and there had been widespread criticism of both the action taken and the manner in which it was carried out.

Further doubt on the validity of the CSM's action was cast in a letter from Dr Trevor Jones, Director General of ABPI, dated 13 November to the Secretary of State, in which he questioned the decision making process within the CSM on this occasion and suggested that an investigation by the Medicines Commission might be appropriate.

5 Response to complaint

The company submitted that the statement in its "Dear Doctor" letter "We remain confident in our products and their risk-benefit profile ..." was not promotional. The confusion which followed the CSM press release and CSM letter had been described in detail above. The CPMP press release of 27 October ended with the following point:

"The CPMP asked its chairman to make this position statement available to the public".

In order to ensure maximum clarification of the CPMP position statement and to reassure doctors and their patients, Organon sent out the "Dear Doctor" letter of 1/2 November. This was not intended as a promotional exercise but to mitigate the alarm and confusion caused by the CSM. It was also apparent that the CSM and the CPMP must have confidence in the products, and their risk-benefit ratio, otherwise they would have instructed their withdrawal from the market. In short, Organon did not believe that the wording used was a claim for the products, but a statement of fact.

Clause 7.3 of the Code required that any claim must be capable of substantiation. Even if the wording was regarded as a claim, Organon did have confidence in Marvelon and Mercilon based on the whole risk-benefit profile, and not only the risk of venous thrombosis as highlighted by the CSM. The three epidemiological studies which were still being analysed would also assess the risks of myocardial infarction and stroke in pill users, and these might be shown to be greater in the "second generation" pills.

This confidence in Organon's products was borne out by the considerable body of available additional data. The CSM press release and letter referred only to one specific risk and did not consider the risk-benefit profile as a whole. Furthermore, Dr Hershel Jick of the Boston Collaborative Drug Surveillance Program, who was responsible for one of the studies involved, had stated in a letter to Organon that:

"..... it may be premature to conclude that third generation oral

contraceptives compared to older contraceptives confer an increased risk for

cardiovascular illnesses as a group".

With regard to the statement "... acted hastily in issuing advice to doctors on unpublished, unreviewed and incomplete studies", Organon submitted that the view that the CSM had acted with haste had been supported by many experts who had been quoted in the media. Further support was given by Dr Trevor Jones, who in his letter to the Secretary of State, asked:

"Why was it necessary for the MCA to act in such haste between the first meeting with the licence holders ... and the publication of the "Dear Doctor/Pharmacist" letter".

Professor W Spitzer, who was responsible for one of the three studies concerned, said in a letter to the BMJ, that:

"... the associations shown do not justify haste in decision making"

In addition, Dr Susan Jick of the Boston Collaborative Drug Surveillance Program had commented to the BMJ that:

"... the whole [CSM] decision is premature".

The speed with which the CSM sent out its letter and press release was obvious from the timings outlined earlier. It also appeared that the MCA did not wait for the CPMP meeting on 18 October to conclude before distributing the letter which was certainly written before the CPMP had met. The premature nature of the CSM's action was further confounded by the decision reached by the CPMP and the following statement in its press release of 27 October:

"During its plenary session on 17 and 18 October, the CPMP held prèliminary discussion and heard the investigators involved in these 3 studies ... CPMP members were asked to analyse the data ... and national competent authorities were asked to wait until further common agreement had been reached by the CPMP before taking any national position".

It was obvious that the CSM totally ignored this plea.

In addition, the complainant claimed that the CSM accepted unpublished, unreviewed and incomplete data in support of product licence applications. In fact the CSM would not consider basing marketing approval on data from an incomplete study, and certainly not in a situation where the CSM had only hours, at most, to consider the data. Any application based on interim, incomplete data would be rejected and cause considerable loss of confidence in the submitting company. Furthermore, in this instance the experts involved in two of the studies (Jick H. and Spitzer) did not advise publication based on their data.

With respect to Clause 8.2, the statement actually supported the scientific opinions of a substantial number of informed health professionals, and it was substantiated by the quotes above. In this instance the CSM appeared to be in a minority and the consensus of clinical opinion from people who had seen the data tended to agree with Organon's statement. Organon therefore argued that there had been no breach of Clause 8.2.

Finally, Organon did not consider that any discredit had been brought to bear by its actions. In fact, it was the actions of the CSM which had discredited the UK regulatory authority, which in areas other than pharmacovigilance enjoyed an excellent reputation.

This was highlighted by Dr Trevor Jones who had said:

"The recent events ... have caused uncertainty and some loss of confidence in their post-licensing activity"

PANEL RULING

The Panel considered that the "Dear Doctor" letter sent by Organon had to be regarded as promotional in nature. It could not be said to come within any of the exemptions in Clause 1.2. Its effect was to support the continuing use of the products concerned, Marvelon and Mercilon. It was accordingly ruled to be in breach of Clause 4.1 because of the lack of prescribing information.

The Panel considered that the circumstances were unusual and that it was not unreasonable for Organon to write to doctors about the matter. The Panel accepted Organon's arguments in support of the content of the letter with regard to the statements concerning the risk benefit ratio and the criticisms of the CSM advice. The statements had been substantiated and did not disparage the opinions of members of the health professions. The Panel therefore ruled that there had been no breach of Clauses 7.3 or 8.2. The Panel did not consider that the letter had brought discredit upon the industry and ruled

that there had been no breach of Clause 2.

APPEAL BY THE COMPLAINANT

The complainant appealed the Panel's ruling of no breaches of Clauses 2 and 8.2 in relation to the allegation that the letter disparaged the opinions of members of the Committee on Safety of Medicines on the following grounds:-

1 The "Dear Doctor" letter criticised the CSM's opinion and Organon's response to the complaint used the phrase "farce" to describe the sequence of media events that resulted from the CSM advice. In addition, the letter sought to undermine the CSM by extolling the virtues of the CPMP in deciding to delay any action. The complainant said that neither himself nor, he thought, most doctors in this country had much idea of the functions or power of the CPMP, but Organon's letter seemed to imply that the latter was better qualified to make decisions than the CSM. The complainant thought this mischievous. He also thought that the Panel's support of this created an unwise precedent.

2 Organon's letter criticised the CSM for acting on unreviewed studies, but in its defence Organon quoted the statements of Professor Spitzer and Dr Jick, who had responsibility for the actual studies. It could not be argued that these two investigators were impartial and it was not clear to the complainant whether these studies were sponsored by oral contraceptive manufacturers or not. Organon had failed to answer the point that the CSM frequently had to review unpublished reports of, for example, toxicological data which pharmaceutical companies did not wish to publish at that stage.

3 The Panel had not referred to the fact that the UK was not unique in expressing its concerns about the study results and the complainant referred in detail to a part of the news section of the BMJ, dated 16 December.

4 It seemed a pity that Organon sought to involve Dr Trevor Jones in this affair as it further confused the issue concerning the impartiality of the Code of Practice Authority *vis-à-vis* the ABPI.

In responding to the above letter, the Authority said, in relation to Point 4, that the views expressed by Dr Trevor Jones, Director General of the ABPI, did not compromise it. The Authority paid Dr Jones' views on the matter neither more nor less attention as a consequence of the relationship between the ABPI and the Authority. The Authority operated separately from the ABPI and did not report to Dr Jones.

RESPONSE

1 Organon emphasised that at no point had it criticised the opinion of the CSM. Any criticism was aimed purely at the procedures involved. Organon believed that the CSM had acted with undue haste.

The effects of the health "scare" were already being seen in the UK. Many women were so concerned by the nature of the warnings that, against all advice, they discontinued the use of their oral contraceptive and some had subsequently had unprotected intercourse. This was reflected in the increases already noted in abortions performed in December/January - it was too early yet for actual figures - and a corresponding rise in the birth rate was expected in July to September 1996. Those pregnancies, both those terminated and those proceeding to term, would carry with them well established rates of morbidity and mortality. The risk per woman year of venous thromboembolism occurring during pregnancy was 60 in 100,000; the corresponding risk reported for oral contraceptives containing desogestrel or gestodene was 21.3 per 100,000. It was these regrettable effects on the women concerned anticipated by Organon last October, that the company sought to prevent. Unfortunately the damage had already been done.

The CPMP was a pan-European body comprising experts drawn from each member state, including two from the UK, and its power in many cases overruled that of the CSM. Many instances already existed which demonstrated this hierarchy and therefore it was not possible for Organon to set an "unwise precedent".

The "Dear Doctor" letter sought to support the authority of the CPMP where there was a need to become accustomed to joint European action on licensing and pharmacovigilance. In this case, a strict legal interpretation of the CSM *vis-à-vis* the CPMP was still awaited.

2 Professor Spitzer's transnational study was sponsored by Schering AG which undertook the study at the request of the (then) BGA [the former German regulatory body], which wanted more data on the incidence of venous thrombosis in women taking oral contraceptive pills containing gestodene. Professor Spizter was asked to carry out the study because of his international reputation as an independent and well respected epidemiologist. It was not to be expected that he would jeopardise this reputation by acting in anything but an eithical and impartial manner. The Drs Jick were apparently asked to carry out their UK study by the CSM and no sponsorship from Organon, Wyeth or Schering was involved. Indeed, from the time that this study was initiated, up until 13 October 1995, there was no communication between Organon and the CSM on this study or any of the studies.

The professional integrity and reputation of the investigators concerned was such that, by implying that they were not impartial, the complainant was actually denigrating their ethical conduct and disparaging their clinical and scientific opinions. Jick and Spitzer did not advise against publication because they did not like their results, but because they were concerned that interim results, which were not completely analysed, could be misinterpreted.

Organon failed to see how the complainant could persist in claiming that it had not answered the point that the CSM frequently has to asssess unpublished reports. The CSM would not accept incomplete study results as supporting data for a marketing authorization. Neither would any company consider submitting such results - any submission which included such deficient data would be rejected by the MCA even prior to consideration by the CSM. The issue was not one of published versus unpublished data, but more importantly action based on validated or unvalidated data. Any decisions which were taken regarding a product were based on a careful and thorough risk/benefit analysis.

3 Point 3 of the complainant's appeal referred entirely to

events which occurred after the circulation of the "Dear Doctor" letter on 1 November 1995 and was therefore irrelevant. The company did, however, provide detailed comment.

4 Organon had not "sought to involve" Dr Trevor Jones in this issue. His letter to the Secretary of State was written without the collaboration or knowledge of Organon and was just a further example of an expert with a high profile position in the industry who shared Organon's view that the safety alert decision-making process and procedures within the MCA required some attention.

Organon wished to re-emphasise that it stood by its belief that it had not breached Clauses 2 and 8.2 of the Code. At no time had it intentionally or unintentionally, brought discredit upon, or reduced confidence in, the pharmaceutical industry. It actually sought to restore confidence which had been diminished. Neither did it disparage the clinical or scientific opinions of members of the health professions, but aimed to clarify a confused situation.

APPEAL BOARD RULING

The Appeal Board considered that the letter had been acceptable in the circumstances pertaining at the time of its issue. It was not disparaging and nor did it discredit the pharmaceutical industry. The Appeal Board accordingly ruled that Clauses 2 and 8.2 of the Code had not been breached. The appeal therefore failed.

Complaint received 8 November 1995

Case completed 28 February 1996

CASE AUTH/371/11/95

PHYSICIAN SUPERINTENDENT/MEDICINES CONTROL AGENCY v LILLY

Advance information about an unlicensed product, Zyprex

The Medicines Control Agency (MCA) referred to the Authority a complaint which it had received from the physician superintendent/clinical director of an NHS trust concerning advance notification sent by Lilly Industries Limited regarding the introduction of Zyprex. The complainant was concerned about this form of publicity, the first in his experience to be so explicit and potentially misleading. The material seemed to the MCA to be unnecessarily comprehensive simply to provide information on a new product in line with the ABPI Guidelines.

The Panel considered that it was difficult to see that there were any significant budgetary implications as the material stated that the cost per day of Zyprex would be between those of clozapine and risperidone and this meant that the material should not have been sent at all. Quite apart from the question of whether anything should have been sent at all, the Panel considered that too much information had been given on the comparative merits of the new product and existing products and that the material as a whole went beyond that permitted. The Panel ruled that the material promoted an unlicensed product in breach of the Code.

COMPLAINT

The MCA had received a complaint from the physician superintendent/clinical director of an NHS trust about advance notification of the availability of Zyprex received from Lilly Industries Limited and had referred the matter to the Authority.

The MCA said that the product did not hold a marketing authorization nor, as the literature explained, had an application yet been made to the MCA. Promotion of an unlicensed medicine was an offence under Regulation 3 of The Medicines Advertising Regulations (SI 1994 No 1932). Whilst the material was not directly promotional, in the MCA's view it did seem to be unnecessarily comprehensive simply to provide advance information of a new product in line with the ABPI Guidelines.

The doctor concerned said in his letter to the MCA that he was concerned about this form of publicity and considered it to be misleading. He was really quite taken aback by the literature, the first in his experience to be so explicit and potentially misleading. In the covering letter and at a few points within the accompanying literature it was clearly stated that the product did not yet hold a UK product licence, but the strong overall implication was that early approval was anticipated. The SPC (summary of product characteristics) was given in its entirety and its provisional nature was only indicated by small print at the bottom of each page showing "draft final". The complainant was not sure what the extent of the mailing list had been for the package but at the very least he supposed that medical directors of every trust in the UK with mental health responsibilities would have received one. The official justification was to provide "service planners" with prior notice in order that budgetary planning could take account of the arrival of the new drug. The complainant wondered whether the MCA shared his concern about this publicity device.

RESPONSE

Lilly Industries Limited stated that the provision of information concerning medicines to NHS staff other than medical practitioners was a new concept and was developing rapidly in conjunction with changing administrative arrangements within the health service. There was an increasing need to give advance information to those controlling NHS budgets so that they could plan for the future. This was acknowledged by the ABPI Guidelines which stated that NHS bodies "need to estimate their likely budgets two to three years in advance in order to meet the Treasury requirements and there is a need for them to receive advance information about the introduction of new medicines, or changes to

existing medicines, which may significantly affect the level of expenditure during future years".

When Lilly sent out its advance material in respect of Zyprex, it had considered that it was complying with the ABPI Guidelines. In particular:-

- the product contained a new active substance;
- it had significant budgetary implications as many of the existing therapies to treat schizophrenia had been on the market for a long time and accordingly had a low price;
- the product was at least a year away from launch at the time of the notification: an application for a marketing authorization was only made subsequently;
- Lilly took great care to ensure that the information was directed only to those persons it had identified as having budgetary responsibility; to reinforce this point, the introduction to the notice stated that the sole intention of the mailing was to provide information to planners and that circulation of the documents was to be restricted to hose with forward planning responsibilities;
- Lilly considered that it was sending out only factual information relating to the treatment of schizophrenia and how it was perceived that Zyprex would fit into this spectrum. It was not in the style of promotional material designed to encourage prescription; Lilly emphasised that the product was not yet licensed; Lilly understood that the MCA had not claimed that its material was directly promotional, but only that it appeared to it unnecessarily comprehensive, which would seem to be a difference in interpretation as to a matter of degree only; Lilly thought it preferable to provide a full picture of the product sufficient to allow a full assessment rather than a superficial description which might lead only to further questions; this was particularly so when one was dealing with an established therapeutic field because the details relating to the product were necessary to make a meaningful assessment of the budgetary implications given the availability of other products.

Lilly could not at present see any particular provision of the ABPI Guidelines that it had breached. Given the persons addressed, the date of supply and the nature of the material, Lilly did not believe that the information could genuinely be viewed as an attempt to promote the prescription, supply or administration of the product. It seemed to Lilly that the recipients of this type of information found it helpful and the isolated objection was more likely to reflect a belief that such notifications were intrinsically unjustified, in which case an allegation of promotion prior to licence was all too easy to make.

In this case, the complaint to the MCA suggested that the information was misleading - seemingly because it was detailed and implied that the licence was imminent. Lilly did not accept that the information was anything but factual and no representation was made expressly or by implication as to the imminent grant of a licence. Lilly expressly noted that the application itself had still not been made and therefore any impression of imminent grant arose out of a misreading of the material by the complainant. If the MCA or the Authority now perceived there to be a need to qualify the type or extent of information that could properly be supplied, Lilly would obviously comply with the new requirements but it did not believe that the new requirements should be retrospectively applied so as to render in breach of the Code practices that had been common within the industry and had not raised serious complaint to date.

RULING

The Panel considered that the provision of advance notification about new products was a difficult area. The ABPI Guidelines on advance notification had been issued in 1992 and were to be included in the supplementary information in the 1996 edition of the Code. There had only been two previous complaints, both involving the same material (Cases AUTH/336/9/95 and AUTH/370/11/95). These had only recently been before the Code of Practice Appeal Board and no reports had as yet been published. There were accordingly no precedents to guide companies.

The Panel noted that the mailing, as provided by Lilly, consisted of a letter from Lilly's medical director, a one page document headed "Advanced notice of a new therapeutic option in the treatment of schizophrenia" with the sub heading "Summary" and a list of the contents of the accompanying a grey plastic folder bearing Lilly's logo in red and headed "Advanced notice of a new therapeutic option in the treatment of schizophrenia". Inside this was an eight page document headed "Advance notification of a new therapeutic option in the treatment of schizophrenia" with the sub-heading "Confidential", a request form for further information, an SPC marked at the bottom "Olanzapine/SPC/Draft Final", a patient information leaflet and three clinical papers.

The Panel could not see that there was any real evidence of significant budgetary implications in relation to the introduction of Zyprex. The company had not yet made a firm decision as to its price. The summary one page document and the eight page document both stated that a reasonable assumption would be to use an average price per day of therapy somewhere between those of clozapine and risperidone.

The Panel noted that the eight page document made somewhat critical references to conventional antipsychotic medications and made specific references to the so called "atypical" antipsychotics, clozapine and risperidone, both referred to by generic name and also by brand name, possibly without the consents of the proprietors.

The Panel noted that the Code of Practice Appeal Board had only very recently considered an appeal in the first two cases concerning the provision of advance information about the introduction of a new medicine, both of which related to the same material (Cases AUTH/336/9/95 and AUTH/370/11/95). During the consideration of these cases the Appeal Board had stated that the information provided should have related to the information provider's product without making unfavourable comparisons in respect of another company's product. The Panel noted this decision but also noted that the Appeal Board had not considered the question of the provision of information on already established products in the same therapeutic area in order to place the new product in the context of existing

therapies. That issue had not arisen. The Panel considered that it might be justifiable to include limited factual information about existing products for that purpose.

The Panel was concerned that the SPC had been set out as if it was in fact an approved official SPC for a new product and the only indication that this was not so was the inclusion of the words "Olanzapine/SPC/Draft final" in small type at the bottom of each page. The patient information leaflet did not bear a similar statement itself although the list of contents of the folder referred to both the SPC and the patient information leaflets as being drafts. The Panel considered that by not stating clearly on each document itself that it was a draft, both documents were misleading.

The Panel noted that among the conditions in the ABPI Guidelines were that the introduction of the product had to have significant budgetary implications, the information had to be provided well ahead of the launch date and it had to be directed to those concerned with budgets and not to those who would be expected to prescribe the product. Only factual information could be provided, including an indication of the likely cost and it could not be presented in the style of promotional material.

The Panel observed that the style and appearance of the material was acceptable. It had not been presented in the style of promotional material.

The Panel considered it was difficult to see that there were any significant budgetary implications as the material stated that the cost per day would be between those of clozapine and risperidone and this meant that the information should not have been sent at all. Quite apart from the question of whether anything should have been sent at all, the Panel considered that on balance too much information had been given on the comparative merits of the new product and existing products and that the material as a whole went beyond that permitted. The Panel ruled that there had been a breach of Clause 3.1.

Complaint received 13 November 1995

Case completed 17 January 1996

CASE AUTH/374/11/95

SECRETARY OF A LOCAL RESEARCH ETHICS COMMITTEE v MEMBER COMPANY

The secretary of a local research ethics committee was concerned about a study carried out in general practice by a member company comparing two products. It was alleged that given the open nature of the study and the development stage of the medicine concerned, the study was designed as more of a marketing opportunity than a valid scientific enquiry.

The Panel considered that the design of the study as an open study was not ideal but it accepted that it would be impractical to carry out a double blind study given the delivery mechanism of the medication. The patient numbers, number of recruiting general practitioners and the payments were not unreasonable.

The Panel considered that the study was a valid scientific study and did not constitute disguised promotion. The study did not therefore come within the scope of the Code.

COMPLAINT

The secretary to a local ethics committee was concerned about an open randomised parallel group multi centre study in general practice comparing two products. The study was being carried out by a research company on behalf of a member company.

The research ethics committee was concerned that given the open nature of the study and the development stage of the medicine concerned, the study was designed as more of a marketing opportunity than a valid scientific enquiry.

The complainant had spoken the Medical Director of the ABPI who had advised that the matter be referred to the Authority.

RESPONSE

The company concerned provided detailed information about the study and submitted that it would be difficult to carry it out on a double blind basis due to the method of delivery of the medication. The company considered that, given the product area, patients would be able to detect the difference between active and placebo. Due to this and because most of the information was collected by the patients, the open randomised design was deemed to be the most logical solution.

The company provided copies of correspondence with the Medicines Control Agency in relation to the clinical trial exemption for the product. The Medicines Control Agency had agreed that the study could proceed.

RULING

The Panel noted that the only requirement in the Code relating to clinical assessments and the like was Clause 10.2 which required that such studies must not be disguised promotion.

The Panel considered that the design of the study as an open study was not ideal but it accepted the submission from the company that it would be impractical to carry out a double blind study given the delivery mechanism of the medication. Efficacy was linked not just to the active medicament but also to the properties of the delivery system.

The Panel considered that neither the patient numbers nor the number of recruiting general practitioners seemed

excessive given the data in the statistics section of the protocol.

The Panel considered that the study was a valid scientific study. The payments were not unreasonable given the British Medical Association suggested fees. It was not disguised promotion and therefore did not come within the scope of the Code.

Complaint received 21 November 1995

Case completed 5 January 1996

CASE AUTH/377/11/95

ANON v MEMBER COMPANY

Mailing on a product

An anonymous complaint was received about a mailing sent by a member company. The complainant queried a claim relating to potential savings and alleged that the mailing was an irritant and the prescribing information was not clear.

The Panel did not accept any of the allegations and no breach of the Code was ruled.

COMPLAINT

An anonymous complaint was received about a mailing sent by a member company to certain doctors, healthcare administrators and pharmacists.

The complainant queried one of the claims relating to potential savings alleged that the mailing was an irritant and that the prescribing information was not clear.

RESPONSE

The company provided information relating to potential savings with its product compared to the competitor products.

With regard to the legibility of the prescribing information the company submitted that it was in accordance with the supplementary information to Clause 4.1 of the Code. The typeface was 7 point, the number of characters per line was 76, there was sufficient space between the lines to facilitate the reading and the type style was clear. In addition there was good contrast between the text colour and the background and the headings were emboldened.

In relation to the allegation that the mailing was an irritant, the company submitted that the mailing provided sound financial reasons to support the use of the product. The focus of promotional material on cost savings was now commonplace. The company could not see what other respect the mailing could be considered an irritant.

RULING

The Panel accepted that the company did have data to substantiate the claim. The Panel therefore ruled no breach of the Code.

The Panel considered that the legibility of the prescribing information was at the limits of acceptability but ruled no breach of Clause 4.1 of the Code.

The Panel did not consider that the material was an irritant. In the Panel's view it was no different to the usual type of mailing sent to doctors to promote products. The Panel therefore ruled no breach of the Code.

Complaint received 29 November 1995

Case completed 21 December 1995

CASES AUTH/378/11/95 & AUTH/391/1/96

PARKE-DAVIS & HOSPITAL DOCTOR v JANSSEN-CILAG

Promotion of Topamax

Parke-Davis complained about a number of promotional items for Topamax issued by Janssen-Cilag. A hospital doctor also complained about one of the items at issue.

Use of data in a product monograph was ruled by the Appeal Board to be misleading in that the impression given was that the data were from directly comparative studies and this was not so. The Appeal Board overturned the Panel's ruling of no breach following an appeal from Parke-Davis. A consultant neurologist made a similar complaint about the product monograph.

The Panel ruled no breach of the Code with regard to an allegation that the word "highly" used in the mailing was a superlative.

The Panel ruled that a claim "Another seizure-free day" in a journal advertisement was misleading given that Topamax could not be used in all types of seizures and for all epileptic patients. This ruling was upheld by the Appeal Board on appeal by Janssen-Cilag.

A dosage card was ruled not to be in breach of the Code by the Panel as the indication was not mentioned in the main body of the card. This information only appeared in the prescribing information. This ruling was upheld by the Appeal Board on appeal by Parke-Davis.

1 Product monograph

Attention was drawn to a page in the product monograph (ref 0097513) headed "Topamax and other recently introduced AEDs" (antiepileptic drugs).

The page included four paragraphs of text and two tables. The first table was headed "Studies of Topamax or recently introduced AEDs" and gave information on lamotrigine, gabapentin and Topamax. The second table was headed "Maximum responder rate seen in each study" and also gave information on lamotrigine, gabapentin and Topamax.

Case AUTH/378/11/95

COMPLAINT

Parke-Davis alleged that the page constituted inappropriate comparisons as there were no direct comparative data between lamotrigine, gabapentin and topiramate so such an attempt at a comparison was inevitably misleading. The representation of the data was inaccurate, unbalanced, not objective and exceedingly ambiguous and therefore explicitly in breach of Clauses 7.2, 7.3, 7.6 and 8.2 of the Code. Inclusion of the disclaimer in the text referring to the fact that there were no direct comparisons did not excuse the depiction of data in an inaccurate and misleading way. Clearly, the presentation of the data was intended to make incorrect comparisons between the three products possible and to misinform the medical profession.

Parke-Davis said that the information about Topamax was referenced to a study "TOP1. A meta-analysis of the efficacy of topiramate for secondary generalised tonic-clonic seizures". The data presented for both lamotrigine and gabapentin reflected the responder rates for all seizure types in single studies. A similar analysis of specific patients with secondarily generalised epilepsy for gabapentin would show a 60% reduction in seizure frequency. Not only was the comparison inappropriate, it was factually incorrect and did not compare like with like.

RESPONSE

Janssen-Cilag agreed that there were no direct comparative data for topiramate, lamotrigine and gabapentin. It submitted that the presentation of the data in the product monograph made the point that the information was from three separate studies. This was also reflected in the text "It should be emphasised that the tables below showed separate studies", in the titles of the tables "Studies of Topamax..." and "maximum responder rate seen in each study" (emphasis added) and the fact that separate reference numbers were given for each of the products concerned.

The company anticipated that clinicians would wish to view data on the efficacy of Topamax and other agents recently introduced as adjunctive treatments for partial seizures. In the absence of direct comparative studies, the company searched the literature to find reports of study types now accepted as defining the efficacy of new adjunctive therapies in a placebo setting. It searched for study designs that included a baseline phase, a double blind phase with placebo as a comparator, that were dose ranging with parallel groups and included patients with refractory partial seizures. The search revealed only one such study each for lamotrigine (with two active dose groups) and for gabapentin (with three active dose groups). In order to simplify and fairly present the data from these two studies and the Topamax study (with three active dose groups) the company elected to show the response of that arm of each study showing the maximum responder rate. As the studies were similarly designed, with patients whose pre study seizure control, concomitant medication and response to placebo were broadly comparable, the company considered it appropriate to present the data for clinicians to draw their own conclusions on relative efficacy.

Janssen-Cilag accepted that an error in its referencing occurred as the information for Topamax in the table was referenced to number 25 which was given incorrectly in the product monograph. The correct reference was the Report of Study YD. This had been sent to Parke-Davis. The company apologised for the error.

PANEL RULING

The Panel examined the page in the product monograph and noted that the text stated that "Definitive conclusions

can only be drawn based on the findings of prospective trials that include all agents being compared. Such a trial is yet to be undertaken." and "It should be emphasised that the tables below show separate studies and in none was there a direct comparison of the respective drugs". The text then went on to describe the studies and state that they had been conducted with similar designs and on similar patient populations.

The Panel examined the studies and noted that the lamotrigine study was carried out on patients with partial seizures, the gabapentin study was carried out on patients with refractory partial epilepsy and the Topamax study was carried out on patients with partial onset seizures.

The Panel noted that there was an error in the product monograph in that the referencing of the Topamax study had been given incorrectly. The data shown for Topamax in the tables was taken from study YD and not the study listed in the references in the back of the product monograph.

The Panel considered that given that the data appeared in a product monograph which was a technical booklet providing detailed information on the product, the company had made it sufficiently clear both in the text and in the headings to the tables that the studies were separate studies and not comparative. The Panel decided that the presentation and the use of the data was not unacceptable and therefore ruled no breach of the Code. This ruling applied only to the presentation in the product monograph. Similar information in other promotional material might not be acceptable.

Case AUTH/391/1/96

Following the above ruling of the Panel, a consultant neurologist complained about the tables in the product monograph. The complainant said that it was not possible to ever compare the efficacies of anticonvulsant drugs unless it was done in direct parallel design comparison study. This was because study populations between different units varied considerably. The tables in the product monograph were misleading and gave a poor picture of both lamotrigine and gabapentin. If Janssen-Cilag had picked other studies, a maximum response rate of 67% for lamotrigine and 45% for gabapentin could have been used.

APPEAL BY PARKE-DAVIS IN CASE AUTH/378/11/95

Parke-Davis alleged that the table as depicted in the product monograph was incorrect as it was referenced incorrectly and the correct reference was not included anywhere in the monograph. This was more than a typographical error. Janssen-Cilag had failed to inform Parke-Davis of the error. Janssen-Cilag had also failed to substantiate the claim in breach of Clause 7.4 of the Code. Typographical errors which led the reader to an incorrect conclusion had previously been ruled in breach of the Code.

Parke-Davis alleged that the studies which appeared on page 24 of the product monograph were not appropriate for comparison. The inclusion of the disclaimer in the text could not allow Janssen-Cilag to provide inaccurate, non objective and misleading information. The topiramate study (study YD) which had now been introduced as supporting evidence had not been peer reviewed or published. There was insufficient information in study YD to establish whether the studies were even remotely comparable, for example with regard to patient demographics which was of paramount importance in refractory epilepsy. In the gabapentin studies the patients were highly refractory with a mean duration of epilepsy of 21 years and in whom therapy with the major marketed antiepileptic products had failed. This was one clear and fundamental flaw, the nature of refractory partial epilepsy was such that comparisons between different patient groups could not be made and should not be attempted in such a way as to imply superiority. Only direct head to head comparisons were appropriate.

RESPONSE FROM JANSSEN-CILAG

Janssen-Cilag fully accepted that there were no direct comparison trials for the products in question. This had been highlighted in the text and fully disclosed the nature of the data presented so that readers could draw their own conclusions.

With regard to the erroneous reference, the company submitted that both the erroneous reference and the correct reference were unpublished studies that would be considered as data on file. Thus any requests for substantiation would be via the company's medical information system which screened requests and ensured that the needs of the enquiry were met.

With regard to the information of the patient demographics, the company submitted that it had never received the specific request for this information from Parke-Davis but it had now been supplied.

With regard to the complaint from the consultant neurologist, the company submitted that the papers cited by the complainant were reviewed by the company and rejected on the grounds that they were too dissimilar to its own studies. The lamotrigine paper was a small crossover study of only 24 patients with refractory partial features. The gabapentin paper was a small crossover study of only 25 patients of whom only 18 had refractory partial epilepsy. It was not placebo controlled and the base line seizure rate was one per week.

When compared to the criteria for the included studies (randomised, placebo controlled, parallel groups and dose ranging) it was not hard to see why the studies were discounted.

APPEAL BOARD RULING

The Appeal Board considered that the product monograph was promotional material subject to the Code. The Panel had ruled that the product monograph was not in breach of the Code and not that it was not promotional material.

The Appeal Board noted that the text above the tables included a number of qualifications about the data shown in the tables. The text stated that definitive conclusions could only be drawn based on the findings of prospective trials that included all the agents being compared and that the tables showed separate studies none of which directly compared the respective products. The Appeal Board noted that the maximum responder rates had been

highlighted in the table by the use of bold print.

The Appeal Board did not accept Janssen-Cilag's submission that the studies were broadly comparable. The Appeal Board considered that it was inappropriate to use the data in the tables as the data was not from studies directly comparing the products although they gave that impression. The implication was that Topamax with a maximum responder rate of 47% was superior to lamotrigine with a maximum responder rate of 34% and gabapentin with a maximum responder rate of 26%. The Appeal Board ruled that the use of the data was misleading in breach of Clause 7.2 of the Code. The appeal on this point was successful.

2 "Dear Doctor" letter and mailing

COMPLAINT

Parke-Davis alleged that the use of the word "highly" in a mailing (ref 0097518B) which accompanied a "Dear Doctor" letter (ref 0097518A) in a claim for Topamax as being "Highly effective in secondarily generalised tonic-clonic seizures" was without qualification and was therefore a superlative.

RESPONSE

Janssen-Cilag pointed out that the superlative adjective or adverb was defined as expressing the highest quality or a very high degree of a quality. Clearly "highly" as used in the phrase "highly effective" was not expressing the highest or a very high degree of effectiveness.

The company also drew attention to the supplementary information to Clause 7.8 of the Code which gave the examples of "best, strongest, widest" as grammatical expressions that required caution in their use. "Highly" did not fit grammatically with this list.

PANEL RULING

The Panel noted that under the supplementary information to Clause 7.8 of the Code superlatives were defined as those grammatical expressions which denoted the highest quality or degree, such as best, strongest and widest etc. The Panel accepted Janssen-Cilag's submission that the word "highly" in the claim "highly effective in secondarily generalised tonic-clonic seizures" was not a superlative. The Panel therefore ruled no breach of Clause 7.8 of the Code.

3 Journal advertisement

COMPLAINT

Parke-Davis drew attention to a journal advertisement (ref 0098064) which appeared in the British Medical Journal of 4 November 1995 and clearly stated "Another seizure-free day". No mention was made of the licensed indication as adjunctive therapy in partial seizures and secondarily generalised seizures (approximately 50% of all seizure types). Parke-Davis alleged that Topamax was being promoted for all forms of epilepsy and as monotherapy which was outside the licence.

RESPONSE

Janssen-Cilag submitted that the advertisement included prescribing information and therefore there was no requirement to state the indication. Janssen-Cilag submitted that whenever an indication consisted of separable clinical entities (for example, hypertension - mild, moderate or severe) it had not been necessary to show the restriction to, for example, mild and moderate hypertension, in the copy in journal advertisements when making it clear in the copy that an antihypertensive was being advertised.

PANEL RULING

The Panel noted that the prescribing information stated that Topamax was used as "adjunctive therapy of partial seizures with or without secondarily generalised seizures, in patients inadequately controlled on conventional first line antiepileptic drugs".

In the Panel's view the implication of the claim "Another seizure-free day" was that the product could be used in all type of seizures and for all epileptic patients. This was not the case as Topamax was limited to use as adjunctive therapy of partial seizures in patients inadequately controlled on conventional first line antiepileptic medicines. The claim was too general given the restrictions for the use of the product. The Panel considered that the claim was therefore misleading and ruled a breach of Clause 7.2 of the Code.

APPEAL BY JANSSEN-CILAG

Janssen-Cilag submitted that the full prescribing information was clearly shown on the advertisement and there was no requirement in the Code to state an exact indication in the body text of an advertisement. The claim drew attention to the efficacy of Topamax in reducing seizure frequency and would encourage the clinician to read the prescribing information. The company submitted that it was common industry practice not to reflect the spectrum of an illness in the body text of a full advertisement and provided a number of examples of advertising of other companies' products which it considered were similar to its advertisement in this regard.

APPEAL BOARD RULING

The Appeal Board examined the advertisement and noted that the indications were given in the prescribing information in the advertisement. However, the Appeal Board considered that the first impression of the advertisement was that the product could be used as monotherapy to treat seizures and this was not so. The product was limited to use as adjunctive therapy of partial seizures with or without secondarily generalised seizures in patients inadequately controlled on conventional first line antiepileptic drugs. The claim was too general given the restrictions for the use of the product. The Appeal Board considered that the claim was misleading and therefore upheld the Panel's ruling of a breach of Clause 7.2 of the Code. The appeal on this point therefore failed.

4 Dosage card

COMPLAINT

Parke-Davis alleged that the dosage card (ref 0097517) specified Topamax as add on therapy but no mention was made of the licensed indication for the product. It was therefore misleading.

RESPONSE

Janssen-Cilag's response to point 3 above applied also to point 4.

PANEL RULING

The Panel examined the dosage card which was entitled "Prescriber's Guidelines" and noted that it referred to Topamax as add on therapy. The text did not refer to seizures at all. It referred to the dosages for Topamax and mechanisms of titrating the dose of Topamax when introducing the product. The indication was given in the prescribing information. The Panel considered that it was sufficient to provide details of the indications in the prescribing information as had been done. The Panel therefore ruled no breach of the Code.

APPEAL BY PARKE-DAVIS

Parke-Davis alleged that the dosage card implied that the product could be used for all forms of epilepsy including primary generalised epilepsy which was incorrect in breach of Clause 3.2 of the Code. Parke-Davis considered the indication needed to be accurately defined in order not to mislead.

RESPONSE

Janssen-Cilag submitted that the dosage card was intended to inform as to the appropriate initiation regimen for Topamax once a clinician had made the decision to prescribe for appropriate patients with partial onset seizures. No reference to the indication had been included in the main body as this was not the prime purpose of the piece.

APPEAL BOARD RULING

The Appeal Board noted that the dosage card stated that Topamax was for add on therapy. The indication was not mentioned, neither was the fact that the product was used in epilepsy and nor was there any reference to seizures in the main body of the text. The only information regarding the indication was in the prescribing information which stated that the product was used as "Adjunctive therapy of partial seizures with or without secondarily generalised seizures, in patients inadequately controlled on conventional first line antiepileptic drugs". The Appeal Board agreed with the Panel that, as there was no mention of the indication in the main body of the text, it was sufficient to provide details of the indication in the prescribing information and upheld the Panel's ruling of no breach of the Code. The appeal on this point therefore failed.

Complaints received

Case AUTH/378/11/95	**30 November 1995**
Case AUTH/391/1/96	**31 January 1996**
Cases completed	**27 March 1996**

CASE AUTH/379/12/95

HOSPITAL INFORMATION PHARMACIST v MEMBER COMPANY

Claim on an envelope

A drug information pharmacist complained about a claim on an envelope, expressing concern at the message it was giving which she considered to be blatant and sweeping.

The Panel considered that there was no objection to a statement on an envelope that was designed to encourage its opening, provided that what was said on the envelope was acceptable in its own right, that it clearly related to the contents of the envelope and that it was not misleading.

Having reviewed the claim in question, which did not mention either the product name or the indication, and the contents of the envelope in the light of evidence provided by the company, the Panel considered that it was acceptable and ruled that there had been no breach of the Code.

COMPLAINT

A drug information pharmacist complained about an envelope which bore a claim. The complainant was not sure if claims made on envelopes were subject to any code of practice but she was concerned about the message it was giving and considered that it was blatant and sweeping.

RESPONSE

The company concerned said that it did not believe that the claim on the envelope was in breach of the Code because it was up-to-date, could be substantiated and was not exaggerated. The company submitted evidence in support of the claim.

RULING

The claim on the envelope was clearly designed to encourage recipients to open it and read the contents but the Panel considered that this was not unacceptable, providing that what was said on the envelope was acceptable in its own right and that it clearly related to the actual contents of the envelope. Any statement on an envelope must not mislead as to the contents. Further, any statement on an envelope must not include both the name of a prescription only medicine and its indication. In the present instance, the Panel considered that the claim on the envelope clearly did relate to its contents. No product names or indications were given.

Having reviewed the information made available by the company in support, the Panel decided that the claim on the envelope was not, in the circumstances, unacceptable. The Panel ruled that there had been no breach of the Code.

Complaint received 5 December 1995

Case completed 30 January 1996

CASE AUTH/381/12/95

CONSULTANT IN PUBLIC HEALTH MEDICINE/ MEDICAL PRESCRIBING ADVISER & PHARMACY PRESCRIBING FACILITATOR v PHARMACIA

Temazepam information packs

A consultant in public health medicine/medical prescribing adviser and a pharmacy prescribing facilitator were concerned that a Temazepam Information Pack supplied by Pharmacia Ltd was disguised promotion. In particular they alleged that it was presented in such a way as to emphasise the benefits of temazepam elixir at the expense of references to tablets.

The pack contained two types of material; that aimed at healthcare professionals and that directed at the patient.

The Panel considered that the Temazepam Information Pack was clearly promotional. It was not disguised promotion and so there was no breach of the Code in that regard. A photograph and its legend in material aimed at healthcare professionals was ruled to be misleading as it gave the impression that the only presentations of temazepam were gel-filled capsules and elixir which was not so as tablets were available. With regard to the patient leaflet, although one section was on the limits of acceptability in terms of balance, both temazepam elixir and tablets had been mentioned and the Panel therefore accordingly ruled no breach of the Code.

COMPLAINT

A consultant in public health medicine/medical prescribing adviser, and a pharmacy prescribing facilitator complained about a Temazepam Information Pack (ref P2399/10/95) which they had been sent by Pharmacia Ltd.

The Temazepam Information Pack contained materials for patients and materials for healthcare professionals. The patient materials were a draft patient recall letter asking the patient to contact the surgery for an appointment for review of their prescription of temazepam and a patient leaflet entitled "Temazepam: changes in the use of your medicine". The materials for use by the general practitioner or the practice nurse were a marking system for patient record cards, a booklet entitled "Temazepam: minimising the abuse, maximising the benefits" and a leaflet entitled "Temazepam: Questions and Answers". A covering letter stated that the intravenous abuse of temazepam gel-filled capsules had led the Department of Health to ban general practitioner prescribing under the NHS of gel-filled capsules. This letter went on to briefly outline the use of the Temazepam Information Pack and summarise the role of the elixir formulation in minimising the abuse of temazepam.

The complainants acknowledged that the pack contained much useful information but they were concerned that it was a form of disguised promotion. In particular, they alleged that it was presented in a way which emphasised the benefits of temazepam elixir, manufactured by Pharmacia, at the expense of references to tablets. The complainants acknowledged that references to the tablets were not entirely absent. However most references to tablets and the potential for reducing the abuse by controlling the prescribing of temazepam were subordinate to references to the elixir. In addition, a photograph in the booklet "Temazepam: minimising the abuse, maximising the benefits" only showed those presentations of temazepam manufactured by Pharmacia ie gel-filled capsules and elixir. No tablets were included. The complainants maintained that for the average healthcare professional who would skip through this literature the overwhelming impression given was that the best way to reduce temazepam abuse was to prescribe the elixir. While the complainants acknowledged that the liquid formulation had undoubted advantages in certain patients, more appropriate use of temazepam (ie short term prescriptions for those who really needed it) was arguably the best way to prevent abuse.

RESPONSE

Pharmacia submitted that it could not see how the Temazepam Information Pack in any way could be regarded as unbalanced or as disguised promotion. The pack had been sent to medical advisors and public health directors. In total 360 packs had been distributed.

The patient leaflet "Temazepam: changes in the use of your medicine" had addressed the appropriate

prescription of temazepam in that it stated "Treatment with temazepam should be as short as possible. The length of treatment may vary from a few days to a maximum of four weeks, including the time to taper off the dose. The doctor will then reassess your needs and advise you if you need further treatment." With regard to the choice of formulation, the final section of the patient leaflet was clearly headed "Your medicine is still available as Temazepam Elixir (liquid) or tablets". In every one of the subsequent four paragraphs both temazepam elixir and tablets had been mentioned.

With reference to the "Temazepam: Questions and Answers" leaflet for doctors the following sentence was included: "Tablet and elixir presentations will remain available on NHS prescription in order to ensure patients will continue to receive the medicines they need". In addition to stating that temazepam elixir was the least abusable presentation, the leaflet also suggested caution should be advised when prescribing to patients for whom the prescriber had little information and to patients with a history of drug abuse. Review of repeat prescribing was also advised.

The company submitted that the contents of the booklet "Temazepam: minimising the abuse, maximising the benefits" were predominantly similar to the other documents. Pharmacia suggested however that it was unfortunate that there were no tablets in the photograph in the booklet, only the elixir and the unfilled capsule presentations. The text above the photograph clearly stated however that temazepam was "...currently available in three formulations: a gel-filled capsule, tablets and elixir".

RULING

The Panel noted that the Temazepam Information Pack contained two types of items ie those directed at health care professionals and those directed at the patient.

The Panel did not accept that the Temazepam Information Pack constituted disguised promotion. It was clearly promotional. In the Panel's view recipients would not be misled into thinking that the material was non promotional. The accompanying letter included prescribing information for temazepam elixir which was also given on the material for the health professionals. The Panel therefore ruled no breach of Clause 10.1 of the Code.

The Panel considered that it was perfectly acceptable for Pharmacia to promote temazepam elixir to healthcare professionals. The material needed to be in accordance with the Code. The material did refer to the need for the overall reduction in prescribing of temazepam but was primarily concerned with the advantages of the elixir compared to the tablets which, in the Panel's view, was not unreasonable.

With regard to the photograph in booklet "Temazepam: minimising the abuse, maximising the benefits" the Panel considered that it was misleading for it only to depict the gel-filled capsules and the elixir. The legend below the photograph "The presentations of temazepam: gel-filled capsules and elixir" added to the impression that these were the only presentations available. It should have been made clear either that tablets were available or that the gel-filled capsules and elixir represented only some of the presentations of temazepam available. Although text on the same page referred to the availability of temazepam tablets this did not correct the misleading impression given by the photograph and its legend. The Panel therefore ruled a breach of Clause 7.2 of the Code.

Turning to the patient leaflet "Temazepam: changes in the use of your medicine" the Panel noted that the information pack had given the doctor no instructions or suggestions on how to use the leaflet. In the Panel's view, given the content of the leaflet, it should only be given to patients already receiving prescriptions for temazepam and this was implied by its title. The final section of the leaflet clearly stated that temazepam was still available both as elixir or tablets and that both formulations would be available under the NHS. The Panel expressed reservations however concerning the use of a capital "T" and a capital "E" each time temazepam elixir had been mentioned. The word "tablet" had always appeared in lower case. The Panel noted that it would have been preferable for the word elixir to have also always appeared in lower case. The Panel noted the requirements of Clause 20.2 of the 1994 edition of the Code that information made available to the public must be factual and presented in a balanced way. The Panel considered that the final section of the leaflet was on the limits of acceptability with regard to balance even though both presentations of temazepam were mentioned. Overall the Panel decided the leaflet was not in breach of Clause 20.2 and no breach was ruled.

Complaint received **18 December 1995**

Case completed **12 February 1996**

CASE AUTH/382/12/95

CHIEF PHARMACIST v SERONO LABORATORIES

Letter relating to supply of Curosurf over Christmas

A chief pharmacist alleged that a letter sent by Serono Laboratories to consultant neonatologists was disparaging in that it implied that some pharmacists were incompetent in managing their stocks of Curosurf over the Christmas period.

The Panel ruled that the letter was in breach of the Code as it disparaged pharmcists as a profession and thereby failed to recognise the special nature of medicines and was not in good taste.

COMPLAINT

A chief pharmacist complained about a letter issued by Serono Laboratories (UK) Ltd regarding the supply of Curosurf during the Christmas period (ref PREINF 3A.DOC) .

The letter had been sent to consultant neonatologists in units which used Curosurf urging them to ensure that the hospital pharmacy had ordered extra stocks of Curosurf to see them through the Christmas break. The letter stated that "It has been our experience in the past that some pharmacists regard the suggestion of taking extra stock over Christmas as a last minute marketing exercise. It is therefore important that you contact pharmacy and instruct them to action this request".

The complainant had written to Serono to point out that implanting the suggestion that the pharmacy was not as competent as it should be was not a recommended way to win friends and influence people.

The complainant asked the Authority to remind member companies that such letters were not helpful.

RESPONSE

Serono Laboratories (UK) Ltd although not a member of the ABPI had nevertheless agreed to comply with the Code.

Serono said that it had already been in contact with the complainant and had unreservedly apologised for the tone of the letter which could certainly be interpreted as casting doubt on the professional competence of pharmacists in the eyes of their consultant colleagues.

There had been no intent to offend. The genuine objective had been to ensure that neonatal units held adequate stocks of Curosurf in view of the long Christmas holiday. In previous years, Curosurf had been sent urgently by bike to various parts of the country which caused unnecessary delays in the treatment of respiratory distress in premature infants. Timing of treatment might be critical in a compromised premature baby.

RULING

The Panel noted the requirements of Clause 9.1 of the 1994 Code that all promotion must recognise both the special nature of medicines and the professional standing of the audience to which it was directed and that good taste must be observed in respect of the illustrations, texts and themes of promotional material and activities. The Panel considered that the letter implied that some pharmacists would fail to order sufficient quantities of medicines to see them through the Christmas break which disparaged pharmacists as a profession and thereby failed to recognise the special nature of medicine and was not in good taste. The Panel therefore ruled a breach of Clause 9.1 of the Code.

Complaint received **19 December 1995**

Case completed **25 January 1996**

ASSISTANT PHARMACEUTICAL ADVISER v RHONE POULENC RORER AND MERCK & LIPHA

Provision of a reference quoted in promotional material for Ikorel

An assistant pharmaceutical adviser drew attention to a claim in GP promotional material on Ikorel issued by Rhone-Poulenc Rorer and Merck & Lipha. The claim was referenced to a study which was in Japanese with an abstract and results table in English. The complainant alleged that the paper was inappropriate to support a significant claim.

The Panel had some difficulty in determining that the request was for a copy of the paper and not for substantiation of the claim. The Panel noted that the paper contained an abstract and table of results in English and considered that these provided sufficient information for readers to assess the quality and significance of the data. The reference had been provided in a timely manner and therefore the Panel ruled no breach of Clause 7.4 of the Code.

COMPLAINT

An assistant pharmaceutical adviser at a health agency submitted a complaint about the promotion of Ikorel (nicorandil) by Rhone-Poulenc Rorer Limited and Merck & Lipha Pharmaceuticals. Attention was drawn to a claim "no haemodynamic tolerance problem" which was referenced to a paper by Tsutamoto T *et al*. The paper which had been provided to the complainant was in Japanese with an abstract and a table of results in English. The complainant alleged that this information, provided several months after the product was launched, was clearly inappropriate to support such a significant claim. The paper was faxed to the complainant on 31 October 1995. A breach of Clause 7.4 of the Code was alleged.

RESPONSE

Rhone-Poulenc Rorer Limited replied on behalf of both itself and Merck & Lipha Pharmaceuticals. The material at issue was a "Dear Medical/Pharmaceutical Adviser" letter (ref 4114 and ZZ08054).

The request for the evidence cited in the mailer in support of the claim "... no haemodynamic tolerance problem." was received by E Merck on 31 October as noted in its enquiry log. The cited paper by Tsutamoto T *et al* was faxed to the complainant on the same day. Whilst the cited reference was the original Japanese publication it included an English abstract summarising the methodology and results of the study. The covering letter also indicated that further information could be requested from Rhone-Poulenc Rorer if required.

Rhone-Poulenc Rorer pointed out that this issue had been the subject of previous discussions and correspondence with the complainant. A summary of the information relevant to haemodynamic tolerance was included in a letter of 9 December 1994. In addition, a copy of a more recent paper by Tsutamoto T *et al* (all in English) based on the same patient study as the earlier reference was forwarded at the same time.

Rhone-Poulenc Rorer submitted that the reference cited was provided expeditiously on request, in accordance with Clause 7.4 of the Code of Practice. In addition, a significant amount of information had been provided to the complainant in support of the claim prior to the issue of the mailer under review.

RULING

The Panel noted, from the correspondence between the complainant and the two companies, that it was difficult to determine whether the original request had been for substantiation of the claim or for a copy of the reference cited in the mailing. The Panel noted that the handwritten covering letter from Merck & Lipha which had accompanied the paper when it was sent by facsimile to the complainant stated "Here is a copy of the paper you requested". Rhone-Poulenc Rorer referred in its submission to "The request from [the complainant] for the evidence cited in the mailer in support of the claim ....". The Panel therefore concluded that the request had been for a copy of the reference and not for substantiation of the claim. In this regard the Panel considered that a reference given in promotional material must be relevant and give pertinent support to the claim being made. A cited reference did not need to provide complete substantiation for the claim. It would be possible for additional material to the cited reference to be provided to substantiate a claim. The Panel then went on to consider the reference in promotional material to a paper which was predominantly in Japanese.

The Panel considered that it was not necessary to expect companies to have available full English translations of all foreign language papers cited. There should, however, be a sufficient English component to allow the reader to appraise a paper's quality and significance. The Panel noted that the paper supplied included both an abstract and a table of results in English. It considered that there was sufficient information given in English for readers to assess the data. The paper had been requested from Merck & Lipha on 31 October 1995 and faxed to the complainant on the same day. The Panel considered that the reference had been provided in a sufficiently timely manner and therefore ruled no breach of Clause 7.4 of the Code.

In its consideration of the case, the Panel noted that the complainant had contacted both Merck & Lipha and Rhone-Poulenc Rorer and it considered that the cooperation and communication between the two companies regarding the provision of data to enquirers could be better. The Panel considered that it was not adequate for one company to refer enquirers to the other company for information. The hand written

covering letter from Merck & Lipha which advised the complainant that they should contact Rhone-Poulenc Rorer to see if they had an English translation of the paper, or indeed any other relevant paper in English, was unhelpful.

Complaint received 2 January 1996

Case completed 20 February 1996

CASE AUTH/385/1/96

NO BREACH OF THE CODE

MEMBER OF A MEDICAL RESEARCH ETHICS COMMITTEE v MERCK & LIPHA

Acamprosate study alleged to be a marketing exercise

A member of a medical research ethics committee complained about a study on acamprosate. Members of the committee were concerned about the scientific validity of the study and considered that it might be regarded more as a marketing exercise for the product.

The Panel noted that the study was being conducted at or around the time that acamprosate would be launched. Any study would inevitably have some promotional impact. The Panel accepted that the study was being conducted in an attempt to answer scientific questions and did not consider it to be disguised promotion. There had been no breach of the Code.

COMPLAINT

A member of a committee on medical research ethics complained about a study submitted by Merck & Lipha Pharmaceuticals, "Acamprosate and psychological intervention: an integrated approach for the prevention of relapse in alcohol-dependent patients".

A number of members of the committee had expressed concerns over the scientific validity of the study, including the absence of controls in relation to the study drug, and considered that it might be regarded more as a marketing exercise for acamprosate.

RESPONSE

Merck & Lipha stated that the study (Protocol CAMP/GB/95.1) was part of an international development for acamprosate conducted in a number of European countries.

There were five clearly defined study objectives specified in the protocol. These involved further clarification of the pattern and severity of relapse in patients receiving acamprosate; identification of the suitability of various forms of psychological intervention for adjunctive treatment with acamprosate; demographic data on the different populations of patients seeking treatment across Europe for alcohol dependence; collection of important data on socioeconomic parameters and quality of life.

The total patient population across Europe would be in the region of 2530 alcohol-dependent patients. The UK portion of the study would involve a total 250 patients recruited from a total of approximately 20 centres. The centres would all be specialist hospital units in the field of drug and alcohol dependence.

The study was set up in accordance with Good Clinical Practice for medicinal products in the European Community, and with the Declaration of Helsinki. The study was being conducted under a clinical trial exception (CTX) for which a protocol addition had been approved.

The absence of a control group (placebo or active) was based on various factors:

1 One of the principal objectives of the study was to assess the utility of acamprosate combined with a range of different psychological interventions tailored to specific patient needs. To include a specific randomised placebo group for each intervention in a study with four main treatment arms (with or without attendance to self-help groups) would be almost impossible to control in order to ensure that adequate numbers of patients were recruited in each potential category without introduction of centre recruitment bias and inadequate study power.

2 The study had been specifically designed to provide data which was not available from the 12 placebo-controlled efficacy studies performed across Europe, which formed the basis of the European registration dossier.

3 At the present time there was no marketed drug which could act as an active control and the same problems with regard to study power and randomisation, could also occur.

4 Once the important baseline economic and demographic data were available it would then be possible to design specific controlled studies targeting individual interventions. At the present time there was insufficient information available in the medical literature to design such studies.

Nine clinical assessments (each of approximately one hour) over a six month period were required and the payment equated to £117 per assessment which was entirely in line with the BMA suggested fees for clinical research. Additional costs for items such as pregnancy tests and clinical laboratory tests were met centrally by the company.

The study was managed by the International Clinical Research and Development group which managed all Merck KGaA international phase II-III research in the UK, reporting to Merck KGaA, Germany, and not to the local UK company.

At the present time acamprosate was not marketed in the

UK. A European multi-state registration procedure had been successful and the UK licensing authority granted marketing approval in December 1995.

The study documention was provided.

RULING

The Panel noted that the study had been approved by the Medicines Control Agency under the Clinical Trial Exemption (CTX) Scheme. An amendment to the protocol had also been approved.

The Panel noted that the only requirement in the Code relating to clinical trials and the like was Clause 10.2 which required that such studies must not be disguised promotion.

The Panel examined the study documentation and noted that in the UK approximately 20 centres were to recruit a total of 250 patients. It noted that patients who had failed to achieve abstinence within the two week run in period would be withdrawn and replaced. Concomitant medication could be prescribed. Central nervous medication would be allowed to relieve alcohol withdrawal or other symptoms but would not be prescribed for the purpose of maintaining abstinence.

The Panel was concerned about the absence of any placebo or control group. It was possible that acamprosate would reduce the success rate of psychological intervention. Placebo groups were helpful in demonstrating that a study design was capable of picking up a treatment effect. The Panel noted that earlier placebo controlled European studies had shown the efficacy of acamprosate and that these had formed the basis of the registration dossier.

The Panel noted that the study was being conducted at or around the time that acamprosate would be launched. Any study would inevitably have some promotional impact. Patients were to be studied, and free acamprosate provided, for six months, yet the summary of product characteristics stated that the recommended period of treatment was one year.

The Panel considered that the payments were reasonable given that the BMA suggested fees for participation in clinical trials was £116-50 per hour. The Panel accepted that the study was being conducted in an attempt to answer valid scientific questions. It had some concerns about the scientific basis of the study but did not consider that the study was disguised promotion. The Panel accordingly ruled that there had been no breach of the Code.

Complaint received **8 January 1996**

Case completed **13 March 1996**

CASE AUTH/386/1/96 *NO BREACH OF THE CODE*

BOEHRINGER MANNHEIM v BOEHRINGER INGELHEIM

Promotion of Bonefos

Boehringer Mannheim complained about certain claims in Bonefos promotional material issued by Boehringer Ingelheim. The Panel ruled that the claims "Proven effective in clinical trials - 1600mg Bonefos" and a similar claim were not capable of substantiation. The claims would be taken to mean that there was clinical trial data on Bonefos tables and this was not so. Boehringer Ingelheim appealed this ruling. The Appeal Board did not agree with the Panel's view and ruled no breach of the Code.

The Panel ruled that the claim "A body of evidence supports the use of oral Bonefos 1600mg daily" was substantiated by the data and therefore ruled no breach of the Code.

COMPLAINT

Boehringer Mannheim UK (Pharmaceuticals) Limited submitted a complaint regarding various promotional items used by Boehringer Ingelheim Limited in the promotion of Bonefos.

The promotional items were a detail aid headed "When life isn't fair" (ref HD1520 Oct 95), a leaflet "Multiple myeloma clinical trial summary" (ref HD1508 Sep 95) and a second leaflet headed "When life isn't fair" (ref HD1509 Sep 95).

Boehringer Mannheim referred to a previous case, Case AUTH/326/8/95, concerning a complaint between the same companies about the promotion of Bonefos. The Panel had made a comment in the case report for Case AUTH/326/8/95 that the claim "Proven effective in clinical trials - 1600mg Bonefos" should be substantiated by data from clinical trials on the product being promoted, Bonefos 1600mg, and this did not appear to be so. It was not sufficient to support the claim as worded with data on another version of the product albeit bioequivalent to the product being promoted. This had been mentioned in the complaint but had not been formally alleged. The Panel had requested that both parties be advised of its views.

Boehringer Mannheim had taken up the claims "Proven effective in clinical trials - 1600mg Bonefos", "Proven effective in clinical trials - 1600mg oral Bonefos" and "A body of evidence supports use of oral Bonefos 1600mg daily" with Boehringer Ingelheim based on the comments made by the Panel in Case AUTH/326/8/95. Boehringer Ingelheim had declined to withdraw the items in question.

Boehringer Mannheim alleged that the claims were in breach of Clause 7.3 of the Code as they were not capable of substantiation and in view of the fact that the Panel had made Boehringer Ingelheim aware of its views in the previous case, it asked that Boehringer Ingelheim be required to withdraw the pieces immediately.

RESPONSE

Boehringer Ingelheim had noted but had not agreed with the Panel's comments in Case AUTH/326/8/95 but had not challenged this view at the time as it was not the subject of a breach of the Code.

The company pointed out that clinical trials of new products were often carried out on small production batches and when scale up of production took place, small changes to the formulation and manufacture might be needed. In these circumstances, provided bioequivalence had been achieved, the clinical trial data were used and accepted in the support of registration and of promotion. This acceptance of clinical trial data by the licensing authority was similarly the case when it considered applications for generic versions of branded medicines, the clinical data on the branded products being directly applied to the generic version provided bioequivalence had been demonstrated and dosage was the same.

The company submitted that clinical trials supporting the claims in question were conducted with a sodium clodronate formulation contained in both size 00 or size 1 capsules. The formulation for both capsule sizes was the same although the process differed in order to achieve the capsule fill required. In some of the clinical studies both capsule sizes were used and because of comparable bioavailability no distinctions were made between them in the final reports. The original 400mg Bonefos capsule product licence was for the size 00 and this was varied to the size 1 capsule on the basis of essential similarity and bioavailability data. No clinical data were required for this change. Thus the presently marketed capsule was accepted as having the same activity as the earlier capsule and was therefore entirely supported by the clinical trial data referred to in the promotional material.

A further development had been that of a film coated tablet containing 800mg sodium clodronate. This was the subject of a further bioavailability study in comparison with the current capsule formulation and which showed bioequivalence at 800mg according to the accepted standard. The licensing authority had accepted the formulation data and the bioavailability data in issuing a product licence for Bonefos tablets indicating that they had the same clinical effects as the same dosage of the capsule formulation.

Boehringer Ingelheim explained that the complaint arose because Boehringer Mannheim had a product licence for Loron 520 which was granted on the basis of bioavailability data but no clinical data. Boehringer Mannheim had contended that Loron 520 had the same therapeutic effect as demonstrated by the clinical trials of the 1600mg formulation but at a dose of 1040mg. It was a cause for concern that Boehringer Mannheim used the clinical trial data on 1600mg sodium clodronate to support its licence for Loron 520 but disputed Boehringer Ingelheim's use of the same data to support the promotion of 1600mg oral Bonefos.

Boehringer Ingelheim submitted that because of the existence of Loron 520 and because of the Panel's previous ruling of a breach of the Code when general claims of dosage efficacy were made, it had endeavoured to make it clear that clinical trials of sodium clodronate had shown that the correct dosage for Bonefos was 1600mg as confirmed by the licence. The company believed that the juxtapositioning of the name Bonefos and the clinical trial dosage was necessary in order to ensure that prescribers were entirely clear as to the clinically supported dosage for the Bonefos brand of sodium clodronate.

PANEL RULING

The Panel noted its previous comments in Case AUTH/326/8/95 that the claim "Proven effectiveness in clinical trials - 1600mg Bonefos" should be substantiated by data from clinical trials of the product being promoted, Bonefos 1600mg. It was not sufficient to support the claim as worded with data on another version of the product albeit one bioequivalent to the product being promoted.

Turning to the case now before it, the Panel examined the promotional materials and noted that the text referred principally to the tablet formulation. Each piece had a photograph of the tablets and the statement "Two tablets equivalent to four Bonefos capsules" adjacent to the claims "Proven effective in clinical trials - 1600mg Bonefos" or "Proven effective in clinical trials - 1600mg oral Bonefos". The prescribing information in all three pieces referred to the capsule, tablet and ampoule formulations. The Panel noted that the clinical trials had been carried out on sodium clodronate capsules and not on the product principally being promoted, Bonefos 800mg tablets. The Panel noted the submission that when applying for a licence for Bonefos tablets 800mg sodium clodronate, a study showing bioequivalence of the tablet formulation with the capsule formulation had been accepted by the licensing authority as showing that Bonefos tablets had the same clinical effects as the same dosage of the capsule formulation.

The Panel considered that the claims "Proven effective in clinical trials - 1600mg Bonefos" and "Proven effective in clinical trials - 1600mg oral Bonefos" would be taken to mean that there was clinical trial data on the product principally being advertised, Bonefos tablets. This was not so. The clinical trials had been carried out using sodium clodronate capsules. In the Panel's view this was a semantic argument rather than a technical argument. There were no clinical trial data on 1600mg Bonefos tablets and therefore the claims, as worded, were not capable of substantiation. The Panel ruled a breach of Clause 7.3 of the Code. This ruling was appealed by Boehringer Ingelheim.

With regard to the claim "A body of evidence supports use of oral Bonefos 1600mg daily", the Panel did not accept that the way this claim was worded meant that the data had to be on the version of the product principally being promoted. It considered that data on sodium clodronate capsules, together with bioavailability data and the fact that the product was licensed was sufficient to substantiate the claim. The Panel therefore ruled no breach of the Code. This ruling was accepted.

APPEAL BY BOEHRINGER INGELHEIM

Boehringer Ingelheim said that the complaint was general and concerned the nature of products used in clinical trials compared with those used in promotion. The complaint made no specific reference to Bonefos tablets or the way in which the claims were presented.

The company submitted that the promotional pieces were

primarily concerned with oral Bonefos and its use at 1600mg daily and also introduced the new formulation of Bonefos, the 800mg tablets. It was indicated that two tablets were equivalent to four capsules and were thereby suitable to deliver the 1600mg daily sodium clodronate that had proved effective in clinical trials. The emphasis on the oral dosage of 1600mg daily was clear throughout the pieces and nowhere was there any suggestion that the clinical trials were performed with Bonefos tablets.

The company submitted that the Panel had not addressed the original basis of the complaint, that promotional claims should be substantiated by clinical trial data on the product being promoted even where bioequivalence has been demonstrated. Boehringer Ingelheim agreed that there were no clinical trial data on Bonefos tablets but there were clinical trials that showed that oral sodium clodronate was effective at a dose of 1600mg daily. Such a dose could be delivered by Bonefos capsules or Bonefos tablets, both of which were licensed in these terms in spite of the fact that the clinical trials included studies with different formulations from those currently marketed. The licensing authority had accepted that the clinical trials were applicable to Bonefos tablets and capsules alike and thereby accepted that the products were therapeutically equivalent to the clinical trials formulations.

APPEAL BOARD RULING

The Appeal Board noted that often the product upon which clinical trials were carried out would be a different formulation to the marketed product.

The Appeal Board did not agree with the Panel's view that the promotional materials at issue were primarily promoting Bonefos tablets. It accepted the submission from Boehringer Ingelheim that the claims "Proven effective in clinical trials - 1600mg Bonefos" and "Proven effective in clinical trials - 1600mg oral Bonefos" were general claims for the dose of Bonefos at 1600mg and not specific claims for the tablet formulation.

The Appeal Board considered that the claims were promoting a dose of Bonefos at 1600mg which was in accordance with the data sheet for the product. The claims were capable of substantiation and the Appeal Board therefore ruled no breach of the Code. The appeal therefore succeeded.

Complaint received **10 January 1996**

Case completed **28 February 1996**

CASE AUTH/389/1/96

PARKE-DAVIS v JANSSEN-CILAG

Symposium report on topiramate (Topamax)

Parke-Davis complained about a Clinical Courier entitled "Topiramate: New Advances in the Treatment of Epilepsy" sent by Janssen-Cilag.

The Panel decided that the report was promotional for Topamax and therefore needed to comply with the Code. A breach of the Code was ruled as at the time the Clinical Courier was circulated. Topamax did not have a UK licence. The report was also ruled to be misleading as it gave the impression that there were data directly comparing antiepileptic products and this was not so. A third breach was ruled as Janssen-Cilag had not provided substantiation for a claim upon request.

The Panel had given previous consideration to this matter in Case AUTH/378/12/95 in which there had been a number of allegations. The Panel had decided not to make a ruling regarding a Clinical Courier entitled "Topiramate: New Advances in the Treatment of Epilepsy" dated April 1995 as it appeared that there had in fact been no complaint about the Clinical Courier. Both parties had been advised of this view and Parke-Davis had subsequently advised the Authority that it was complaining about the Clinical Courier. It was therefore decided that the matter would be treated as a new case, Case AUTH/389/1/96.

COMPLAINT

Parke-Davis said that it wrote to Janssen-Cilag concerning the Clinical Courier which it considered was an overtly promotional report of Janssen-Cilag's topiramate symposium in Oporto. Parke-Davis alleged that the Clinical Courier constituted promotion of an unlicensed product and made statements relating to the relative efficacy of its product Neurontin (gabapentin) and topiramate. After some delay, Janssen-Cilag's Director of Marketing Planning and Development had agreed with Parke-Davis' concern that there was no direct comparative data between topiramate (Topamax) and gabapentin and had assured the company that this would not be repeated. Janssen-Cilag agreed to provide Parke-Davis with a copy of its letter of apology to physicians.

Parke-Davis alleged that the timing and distribution of the Clinical Courier clearly represented pre-marketing of an unlicensed product in breach of Clause 3.1 of the Code. The item was sent some 7 months after the Oporto symposium and 5 months prior to the launch of Topamax, calculated to ensure substantial exposure amongst UK health professionals prior to the licensing of Topamax in the UK. The Clinical Courier was by no means non promotional and purely scientific in nature and nor was it accurate.

Secondly, the item made reference to a number of marketed antiepileptic drugs and, in particular, was disparaging to lamotrigine and gabapentin. It was stated that the efficacy of topiramate compared favourably to vigabatrin and appeared to be superior to lamotrigine. It also stated that the efficacy of topiramate exceeded that of gabapentin. There was no direct comparative data to substantiate the claim. A breach of Clause 7.2 of the Code was alleged.

The continued delay in responding and lack of adequate action from Janssen-Cilag represented a clear effort to gain marketing advantage ahead of the launch of Topamax. A breach of Clause 7.4 of the Code was alleged. The company had raised its concerns with Janssen-Cilag in June 1995 and received a reply in September 1995 agreeing to send a letter of apology. Even now Parke-Davis had not received confirmation that physicians had been sent a letter. Although a letter was received individually by some Parke-Davis employees on 15 January 1996, this letter was undated and had been sent to a number of individuals who had not even attended the meeting in Oporto.

RESPONSE

Janssen-Cilag said that the Clinical Courier was circulated by its international commercial development department in America to all attendees, regretfully without Janssen-Cilag UK having had the opportunity to review the circulation list. UK attendees did receive the Clinical Courier and the company acknowledged that this should not have happened as at the time there was no UK licence for Topamax. The company was in the process of sending a letter of correction to the UK attendees.

Having read the Panel's initial comments on the point that it might be possible to send attendees a copy of a report from a symposium that they had attended if such a report was non promotional, scientific and accurate, Janssen-Cilag was now the opinion that it might be acceptable to circulate the report to the attendees as they had already been exposed to the information. Accordingly the company refuted the allegation that the distribution of the Clinical Courier was in breach of Clause 3.1 of the Code.

Janssen-Cilag referred to its appeal in the related Case AUTH/378/11/95 (point 1) in response to the alleged breaches of Clauses 7.2 and 7.4 regarding the product monograph in which the company accepted that there was no direct comparative trials for the products in question. The studies quoted were broadly comparable.

RULING

The Panel noted that it would be permissible to send a copy of a report from a symposium to those who had attended the symposium, provided the report was non promotional, scientific in nature and accurate. Distribution of such a non promotional report to people who had not attended the symposium would be seen as promotion.

The Panel now examined the Clinical Courier and noted that it had been sponsored by Janssen-Cilag. It was laid out in a promotional manner with positive features of Topamax highlighted in the text and in the conclusions to each section. The Panel decided that the Clinical Courier was promotional for Topamax and consequently needed to comply with all the relevant requirements of the Code, including the need for prescribing information. The Panel noted that the Clinical Courier had been circulated by the international commercial development department of Janssen-Cilag in America. In accordance with the established precedent, as the material had been circulated in the UK, the UK company was held responsible under the Code.

The Panel noted that at the time the Clinical Courier was circulated, Topamax was not licensed in the UK. The Panel therefore ruled a breach of Clause 3.1 of the Code.

The Panel considered that the comparison of topiramate with gabapentin and felbamate was misleading as there was no data directly comparing the products although this was the impression given in the Clinical Courier, for example by the claim "The efficacy of topiramate exceeds that of gabapentin or felbamate". A breach of Clause 7.2 of the Code was ruled.

The Panel noted that Parke-Davis had asked Janssen-Cilag for data to support the claim that "The efficacy of topiramate exceeds that of gabapentin or felbamate" which appeared as a conclusion in the report of a presentation. No such information had been provided. Parke-Davis had also queried whether the presentation had come to any such conclusion. The Panel noted that substantiation had never been provided by Janssen-Cilag and therefore ruled a breach of Clause 7.4 of the Code.

Complaint received **30 January 1996**

Case completed **27 March 1996**

CASE AUTH/390/1/96

CONSULTANT PHYSICIAN/GASTROENTEROLOGIST v WYETH

Zoton press release

A consultant physician/gastroenterologist alleged that a Zoton press release issued by Wyeth Laboratories distorted what he had written and did not reflect his views about a competitor product.

The Panel ruled that the press release was in breach of the Code as it was misleading in that it did not reflect the complainant's view.

COMPLAINT

A consultant physician/gastroentorologist, complained about a press release issued by Wyeth Laboratories referring to the use of Zoton 15mg (lansoprazole) as maintenance treatment in reflux oesophagitis.

The complainant said that the press release contained the following statement concerning omeprazole (Losec) as maintenance therapy for reflux oesophagitis "Reporting a 50% endoscopic relapse rate for the 10mg dose, [he] suggested that this dose may be suboptimal as maintenance therapy compared with 20mg". The complainant said that this distorted what he had written and did not reflect his views. His original statement had been "The 20mg dose may be effective in patients for whom 10mg is suboptimal".

The complainant said that the study referred to the optimal maintenance dose of omeprazole in reflux oesophagitis patients studied for one year, or until symptomatic relapse. As far as he was aware, there was no directly comparable study with 15mg of lansoprazole. If such data did exist, he would welcome sight of them.

RESPONSE

Wyeth provided copies of two press releases which had been issued together and sent to the medical, pharmaceutical and lay press. A circulation list was provided. The first was headed "Zoton (lansoprazole) 15mg for maintenance treatment of reflux oesophagitis" and included the statement in question. The second was headed "A background to reflux oesophagitis and its treatment".

Wyeth accepted that there might have been an inadvertent misrepresentation of the complainant's views and to that extent it agreed that Clause 7.2 had been breached. The company pointed out that the statement complained of was not a direct quotation and therefore Clause 11.2, which applied specifically to the use of quotations, had not been breached.

Wyeth also provided a copy of a letter it had sent to the complainant about the matter in which Wyeth stated that it was fair to say that the paper indicated that the 10mg dose of omeprazole might be suboptimal in some patients and that the 20mg dose might be more effective in those patients. This was the message that the company was trying to convey in the press release. The company accepted that the complainant did not go so far as to draw a general conclusion that 10mg dose might be suboptimal. The company did not intend to misrepresent his views but to the extent that this had occurred the company apologised unreservedly.

RULING

The Panel noted that the disputed statement had not appeared in the press release as an actual quotation attributed to the complainant and therefore Clause 11.2 did not apply. The Panel noted that the complainant had not suggested that the 10mg dose of omeprazole might be suboptimal as maintenance therapy compared with a 20mg dose as stated in the press release but that the 20mg dose might be effective in patients for whom the 10mg dose was suboptimal. The Panel considered that the press release was misleading as it did not reflect the complainant's views. The Panel therefore ruled a breach of Clause 7.2 of the Code.

Complaint received **31 January 1996**

Case completed **11 March 1996**

Case AUTH/393/2/96

SEARLE v PFIZER

Cost comparison in an advertisement for Feldene Gel

Searle alleged that a cost comparison in an advertisement for Feldene Gel issued by Pfizer was misleading because it was based solely on the maximum recommended dose and did not take into account variability in usage rates.

The Panel made a number of observations about the chart and decided that the comparison was too simplistic. The Panel ruled a breach of the Code as it was misleading to compare the products on a maximum daily dosage basis.

COMPLAINT

Searle submitted a complaint regarding a journal advertisement for Feldene Gel (ref 42812) issued by Pfizer Limited which appeared in Medendium, Autumn 1995.

The advertisement consisted of a cost comparison of Feldene with six other topical non steriodal anti-inflammatory drugs (NSAIDs). For each product, the material gave the product name, which appeared on part of a tube, a daily dosage and the cost of the daily dosage. The costs ranged from £1.12 for diclofenac gel (Voltarol Emulgel) to 28p for Feldene Gel. Below the data was a statement "Prices calculated at maximum recommended dose". The advertisement included the claim "More medicine for your money than most other topical NSAIDs" and, next to the picture of a Feldene Gel tube, the claim "28 days treatment for only 28p a day at the maximum recommended dose". The prices were from MIMS June 1995.

Searle alleged that the cost comparison was misleading because it was based solely on the maximum recommended dose and did not take into account the variability in usage rates. By implication, the advertisement was claiming that Feldene Gel was more potent than the other NSAIDs named in the advertisement which was a claim that Pfizer had been unable to substantiate. A breach of Clause 7.2 was alleged.

RESPONSE

Pfizer submitted that the advertisement clearly stated that the cost comparison was based upon the maximum recommended dose. The comparison used data given in the products' approved labelling and the listed prices of the products. There was no mention or claim in the advertisement, or any such implication, concerning the relative potencies of the products.

Pfizer submitted that the advertisement was a fair comparison, using relevant data for the product group and did not mislead either by content or implication.

RULING

The Panel made a number of observations about the advertisement.

The Panel first noted that, according to the product data sheets, there were a number of preparations listed in the chart which should only be used for a limited time period. For example, ketoprofen gel (Oruvail Gel) should only be used for up to seven days, it was recommended that treatment with benzydamine hydrochloride cream (Difflam) was limited to no more than 10 days, treatment with felbinac (Traxam) had to be reviewed after 14 days use and it was recommended that treatment with diclofenac gel (Voltarol Emulgel) be reviewed after 14 days use or in oesteoarthritis after 4 weeks use. The Panel considered that the inclusion of the claim for Feldene Gel that "28 days treatment for only 28p a day at the maximum recommended dose" might give the impression that all the products in the chart could be used for 28 days treatment which would not be consistent with the data sheet limitations noted above. Further, the products did not all have the same indications. For example, Feldene Gel was licensed for osteoarthritis and acute musculoskeletal disorders whereas a number of the other products such as Oruvail Gel and Difflam Cream were only licensed for short term relief of musculoskeletal pain and inflammation.

Secondly, the Panel noted that the cost of the whole tube was a relevant factor given that one tube was likely to be the usual prescription. A number of the products on the chart were priced at £7 for 100g (Voltarol Emulgel, Difflam and Traxam). Oruvail Gel cost £6.78 (100g), mucopolysaccharide and salicylic acid cream (Movelat) cost £4.14 (100g), ibuprofen cream (Proflex) cost £6.50 (100g) and Feldene Gel was £7.84 (100g) for 112g which was equivalent to £7 for 100g. The daily cost given in the chart would only be a relevant method of quantifying the cost if patients were using the product long term and needed more than one tube to treat the condition.

Thirdly, the advertisement compared the maximum daily doses of the topical NSAIDs and the Panel was not satisfied that this was fair. A treatment that might be the most expensive on a daily basis could be the cheapest to treat a particular condition if it only needed to be used for a short time period. Given the nature of the products, usage rates would tend to be imprecise. The Panel did not accept that the advertisement implied that Feldene Gel was the most potent of the NSAIDs.

Fourthly, the Panel noted that the products listed in the chart had a range of doses. There was no way of calculating how long a tube of Movelat or Proflex would last as the dose was given in centimetres unlike the other products. It was not clear how the daily cost had been calculated for these products. It would have been helpful to have given the dose in grammes.

Finally the Panel noted the claim "more medicine for your money than most other topical NSAIDs" which could be taken to imply that Feldene Gel gave more weight for its cost than the other products. This was not so as Voltarol Emulgel, Difflam, Traxam and Feldene Gel all cost 7p per gramme. The other products cost less with Movelat costing only 4.14p per gramme.

The Panel noted that it was very difficult to present a fair cost comparison of topical products. Pfizer had tried to comply with the Code in this difficult area. The claim made related to the price of a day's treatment for each product based on its maximum dose. The Panel did not accept that the comparison was fair as no allowance had been made for differences between the products listed.

The Panel considered that the comparison was too simplistic. It considered that it was misleading to compare the products on a maximum daily dosage basis. The Panel therefore ruled a breach of Clause 7.2 of the Code.

Complaint received **1 February 1996**

Case completed **28 March 1996**

CASES AUTH/395/2/96 & AUTH/405/2/96

MERCK & LIPHA AND GENERAL PRACTITIONER v SCHERING HEALTH CARE

Promotion of Progynova TS

Merck & Lipha alleged that claims made by Schering Health Care that its product Progynova TS was the "first 7 day HRT patch" were misleading. A similar complaint was made by a general practitioner.

The Panel considered that, given the general nature of the claims, the audience would take them to mean that Progynova TS was the first seven day patch available for prescription in the UK. In the Panel's view this meant that the product that was delivered to wholesalers first should be regarded as the first product available provided its availability was made known. The Panel considered that Progynova TS was not the first seven day HRT patch to be available. The claims as worded were misleading in breach of the Code.

Case AUTH/395/2/96

COMPLAINT

Merck & Lipha Pharmaceuticals complained about the promotion of Progynova TS by Schering Health Care Limited. The material at issue was an advertisement for Progynova TS in Pulse, 25 January 1996, which stated "Progynova TS - the first 7 day HRT patch", a "Dear Doctor" mailing received in the week ending 26 January which included the statements "will be available" and "first 7 day patch" and an advertisement in GP, 1 February 1996, which stated that the product was available in "two strengths" and was "The first 7 day HRT patch".

Merck & Lipha said that based on the sequence of the material, it would appear that Progynova TS was launched and became available for prescription on or after 1 February 1996. The company had been unable to obtain the product on 1 February from various wholesalers and retailers. In contrast, its own product, Femseven, a seven day HRT patch, was available for prescription from 31 January and had been available from wholesalers from 23 January. Data was provided to support this point.

The company alleged that the claims made by Schering that its product was "the first 7 day HRT patch" were in breach of Clause 7 of the Code.

Case AUTH/405/2/96

A general practitioner pointed out that in MIMS February, two HRT patches had been launched, both of which were active for seven days. The complainant had noticed in the GP tabloids that one of the patches, Progynova TS, was described as being "the first 7 day HRT patch". Since medical practitioners were informed of the existence of the two rival products at the same time, could this patch truly be the first seven day patch?

The complainant assumed that one patch was released for sale a day or two ahead of the other. However, the date on the advertising for the Femseven patch (Merck & Lipha's product) appeared to be December 1995 and that of Progynova TS January 1996. The complainant was curious as to how it could be established which was the first seven day patch.

RESPONSE

Schering Health Care Limited pointed out that its seven day patch, marketed as Climara had been available in the United States since May 1995. It was therefore the first seven day patch in the world. The product licence for Progynova TS was dated July 1995. The company was confident that the licence to market its seven day patch was the first in the UK.

The company submitted that it had made the claim openly in widely distributed literature that it was the first seven day patch and informed health professionals of its forthcoming launch in good faith. The company understood that the Merck & Lipha product was to be launched on 5 February 1996. Had Merck & Lipha informed healthcare professionals as openly as Schering had done of its plans, Schering would have been in a position to give consideration to qualifying the claim. The company surmised that Merck & Lipha brought their launch date forward ahead of its own as a piece of commercial mischief.

With regard to the complaint from the general practitioner, the company noted that the complainant was referring to the dates of preparation of the advertisements which, of course, applied to the advertisements and not to the products and were therefore irrelevant in the context of the issue of which was the first product.

The company provided proof of delivery of Progynova TS on 5 February 1996 to a wholesaler.

RULING

The Panel did not accept the submission that the claims at issue, principally "Progynova TS - the first 7 day HRT patch", would be taken as meaning either the first seven day patch available in the world or the first seven day patch to be granted a UK product licence. The Panel considered that, given the general nature of the claims, the intended audience would take them to mean that Progynova TS was the first seven day patch available for prescription in the UK. In the Panel's view, this meant that the product that was delivered to wholesalers first should be regarded as the first product available for prescription in the UK provided its availability was made known. The Merck & Lipha product was available from wholesalers from 23 January 1996, whereas the Schering product was available from 5 February 1996. Both were referred to as new products in the February edition of "MIMS". The ABPI had received its copy on 2 February 1996. The Panel considered that the Merck & Lipha Product was the first seven day HRT patch to be available in the UK. The Panel considered that the claims as worded were misleading and therefore ruled a breach of Clause 7.2 of the Code. This ruling applied to both cases. The dates on the advertisements were not relevant.

Complaints received

Case AUTH/395/2/96	**5 February 1996**
Case AUTH/405/2/96	**21 February 1996**
Cases completed	**25 March 1996**

CASE AUTH/396/2/96

ORGANON v NOVO NORDISK

Kliofem journal advertisement

Organon Laboratories alleged that a strap line in an advertisement for Kliofem issued by Novo Nordisk, "Period-free HRT that postmenopausal women prefer", was ambiguous as it could be taken to mean "THE period-free HRT that postmenopausal women prefer", implying a preference over other bleed free regimens. There were no data to substantiate such a claim. Organon also alleged that the strap line was disparaging because it implied that women prefered Kliofem over other period-free HRT preparations.

The Panel considered that the strap line was ambiguous as it could be interpreted in two different way. The Panel's view was that it would usually be taken to mean that women preferred Kliofem to other bleed free preparations but there were no data to substantiate that interpretation. Breaches of the Code were ruled. The Panel did not consider that the strap line was disparaging of other period free HRT preparations.

COMPLAINT

Organon Laboratories Limited complained about a Kliofem journal advertisement (KLI 96/18) issued by Novo Nordisk Pharmaceuticals Ltd. Novo Nordisk was not a member of the ABPI but had nevertheless agreed to comply with the Code.

Organon alleged that the strap line "Period-free HRT that postmenopausal women prefer" was ambiguous in breach of Clause 7.2 of the Code. It was likely to be interpreted as "THE period-free HRT that postmenopausal women prefer" implying a preference over other "bleed free" regimes.

Organon also alleged that the strap line was not capable of substantiation in breach of Clause 7.3 as the study cited by Novo Nordisk made no comparison between different period-free preparations but simply compared a conventional "bleeding" therapy with one "period free" regimen.

A breach of Clause 8.1 was alleged as the strapline was disparaging because it implied that women preferred Kliofem over other period-free HRT preparations. There was no evidence to support this implication.

RESPONSE

Novo Nordisk explained that postmenopausal women had been recruited into the largest ever UK multi centre hormone replacement therapy (HRT) study to assess patient preference after nine months of Kliofem therapy. A total of 399 women who had previously been on one of five different cyclical HRT preparations completed the study and of those 83% preferred Kliofem to their previous treatment. 493 who had previously not been treated with HRT completed the study and of those 88% preferred Kliofem to no previous treatment.

With regard to the allegation that the strap line was ambiguous and was likely to be interpreted as "THE period-free HRT...", Novo Nordisk submitted that none of the material inserted "THE" in front of the strap line. The company did not intend to imply that Kliofem was THE period-free HRT as the data would not substantiate that statement.

Novo Nordisk submitted that in the UK there were currently approximately 8 million women over 55 (Kliofem was only promoted to women who were one year postmenopausal) and that only one third of HRT was attributed to this age group. 22 million cycles of HRT were prescribed in 1995 and, consequently, only 633,000 patient years of HRT were actually prescribed in the postmenopausal group. The vast majority of postmenopausal women (71/3 million in the UK) did not take HRT whereas approximately two thirds of a million did. Of these users of HRT in the postmenopausal group, more than 85% used HRT which was not period-free. The preference data, in which a total of 863 postmenopausal women were studied, therefore represented the current status in this group and fully substantiated the strapline.

Concerning the alleged breach of Clause 8.1, Novo Nordisk was curious as to how any disparaging claim could have been made as no other company's products or activities were mentioned in the campaign.

RULING

The Panel noted that the strap line "Period-free HRT that postmenopausal women prefer" was printed directly underneath the most prominent display of the brand name. It was possible to interpret it to mean either that postmenopausal women prefered period-free HRT or that Kliofem was the period-free HRT that postmenopausal women prefered.

Given the positioning of the strap line immediately below the brand name, the Panel considered that the strap line would be taken by most readers to mean that of the available period-free HRT products, Kliofem was the product women preferred. It was, however, somewhat subjective and some readers would doubtless interpret it otherwise. The Panel considered that the strap line was ambiguous as alleged and ruled a breach of Clause 7.2 of the Code.

The preference data submitted by Novo Nordisk in support of its claim involved a study of 399 women previously treated with cyclical HRT and then switched to Kliofem. Patient preference was assessed after nine months of Kliofem therapy. The Panel noted that before being switched to Kliofem therapy all of the women had been on HRT preparations which would give a monthly bleed. The study had not included any bleed free preparations apart from Kliofem. Given the Panel's interpretation that the strap line would usually be read as meaning that Kliofem was the period-free HRT that postmenopausal women preferred this had therefore not been substantiated. The Panel accordingly ruled a breach of Clause 7.3 of the Code.

The Panel did not accept that the strap line was disparaging of other period-free HRT preparations as the implication of the strap line was only that women preferred Kliofem to other period-free preparations. No critical comment was made about other HRT preparations. The strap line could in fact be regarded as a hanging comparison as it was not clear as to what Kliofem was prefered to. The Panel therefore ruled no breach of Clause 8.1 of the Code.

Complaint received **8 February 1996**

Case completed **19 March 1996**

CASE AUTH/397/2/96

HOSPITAL PHARMACIST v DUMEX

Conduct of a representative

The deputy chief pharmacist at an NHS trust hospital complained about a Dumex representative who had asked to check on ward's stock of diazepam rectal tubes, wrongfully claiming that he had an appointment in pharmacy and needed to check their stocks. He had tried to undermine nursing staff's confidence in the product they were using.

The Panel noted the psychiatric problems experienced by the representative concerned but a company had to take responsibility for its representatives while they were acting within the scope of their employment. The representative concerned had failed to maintain a high standard of ethical conduct and a breach was ruled.

COMPLAINT

The deputy chief pharmacist at an NHS trust hospital complained about a representative from Dumex Limited. Dumex Limited was not a member of the ABPI but had nevertheless agreed to comply with the Code.

The complainant said that whilst visiting the hospital the representative had entered a paediatric ward without an appointment and had asked to see their stocks of diazepam rectal tubes. The representative had explained that he had an appointment in pharmacy and therefore needed to check which brand of diazepam had been supplied. The representative did not have an appointment in pharmacy. During his ward visit, the representative had tried to reduce nursing staff's confidence in the product that they were using. He also stated that the pharmacy departments in the district were unnecessarily blocking his attempts to introduce Dumex's product Stesolid and that in effect the pharmacy departments were supplying inferior products.

The nursing and pharmacy staff were extremely uncomfortable with the representative's approach. The complainant was concerned that a number of clauses in the Code had been broken. If there were any subsequent incidents of a similar nature, the Dumex representative would be asked not to visit the hospital thereafter. The complainant had sent Dumex a copy of the hospital's "Guidance for Pharmaceutical Representatives" and asked that it be made available to the representative concerned.

RESPONSE

Dumex Limited apologised to the complainant and other hospital staff on behalf of its representative for any conduct that was deemed unethical or in breach of the Code and it accepted the complainant's record of the events.

Dumex did, however, put forward certain mitigating circumstances in relation to the matter. The representative concerned had suffered a prolonged psychiatric illness during which time he was under medical supervision and prescribed medication. Dumex was fully supportive of him during this period when he was unfit for work. He had returned to work but had ceased employment with Dumex shortly afterwards. Dumex accepted that this explanation did not excuse the actions of its representative but it was offered as background information. Dumex sought to assure the complainant and the Authority that all of its medical sales staff were aware of and trained and briefed to conform with the Code.

RULING

The Panel noted that Dumex accepted the complainant's account of the events as being factual and also noted the representative's illness. It was a clearly established principle under the Code that companies had to accept responsibility for what their representatives did if they were acting in the course of their employment. In this instance, the representative had clearly been acting in the course of his employment and his conduct had not been in accordance with all of the relevant provisions of the Code as required by Clause 15.2. The representative had failed to maintain a high standard of ethical conduct. The Panel therefore ruled that there had been a breach of Clause 15.2 of the Code.

Complaint received **8 February 1996**

Case completed **14 March 1996**

CASES REPORTED IN THIS REVIEW

Reports relating to complaints received prior to 1 January 1996 name the company against which the complaint was made only where a breach of the Code was ruled. As a result of recent changes to the Constitution and Procedure for the Prescription Medicines Code of Practice Authority, all reports relating to complaints received after 1 January 1996 name the company involved regardless of whether a breach of the Code was ruled.

Cases in which a breach of the Code was ruled are given below in bold type.

323/8/95	**Abbott v Pfizer**	**Promotion of Zithromax**	**Breach 7.2**	**No appeal**
336/9/95 **370/11/95**	**Schering &** **Medicines Control Agency** **v Serono**	**Advance information about an unlicensed product interferon beta-1a**	**}** **} Breach 3.1**	**Appeal by respondent**
338/9/95	**Pharmaceutical adviser v Glaxo**	**Zantac detail aid**	**Breach 7.2**	**Appeal by complainant**
342/10/95	**Stiefel v Yamanouchi**	**Bar chart in Dermamist brochure**	**Breach 7.6**	**No appeal**
343/10/95 to 357/10/95	GP v Member companies and non member company	Sponsored articles in a journal	No breach	No appeal
359/10/95 **360/10/95**	**Assistant pharmaceutical adviser v Rhone-Poulenc Rorer &** **Merck & Lipha**	**"Dear Medical/ Pharmaceutical Adviser" letter on Ikorel**	**Breach 7.2**	**Appeals by both complainant and respondents**
361/10/95	**GP v Schering-Plough**	**Market research survey**	**Breach 4.1**	**Appeal by respondent**
362/10/95	**University doctors/Director v Bayer**	**Promotion of Ciproxin**	**Breach 7.2**	**No appeal**
364/10/95	**Parke-Davis v Boehringer Mannheim**	**Bezalip Mono detail aid**	**Breach 4.6 & 7.2**	**Appeals by both complainant and respondent**
366/10/95	**Pharmacist with NHS body v Roche**	**Rocephin journal advertisement**	**Breach 7.2**	**No appeal**
367/10/95 **373/11/95**	**Pharmaceutical adviser & Janssen-Cilag v Schering**	**"Dear Colleague" letter on oral contraceptives**	**Breach 7.2**	**No Appeal**
368/10/95	**National Pharmaceutical Association v Roche**	**Malaria advice leaflet for patients**	**Breach 9.1**	**No appeal**
369/11/95	**Doctor v Organon**	**Letter concerning Marvelon and Mercilon**	**Breach 4.1**	**Appeal by complainant**
371/11/95	**Physician superintendent/ Medicines Control Agency v Lilly**	**Advance information about an unlicensed product, Zyprex**	**Breach 3.1**	**No appeal**
374/11/95	Secretary of a local research ethics committee v Member company	Clinical study on a product	Not within scope of the Code	No appeal
377/11/95	Anon v Member company	Mailing on a product	No breach	No appeal
378/11/95 **391/1/96**	**Parke-Davis &** **hospital doctor v Janssen-Cilag**	**Promotion of Topamax**	**Breach 7.2**	**Appeals by both first complainant and the respondent**
379/12/95	Hospital information pharmacist v Member company	Claim on envelope	No breach	No appeal
381/12/95	**Consultant in public health medicine/medical prescribing advisor & pharmacy prescribing facilitator v Pharmacia**	**Temazepam information packs**	**Breach 7.2**	**No appeal**

382/12/95	**Hospital chief pharmacist v Serono**	**Letter relating to supply of Curosurf**	**Breach 9.1**	**No appeal**
383/1/96 384/1/96	Assistant pharmaceutical adviser v Rhone-Poulenc Rorer & Merck & Lipha	Provision of a reference quoted in Ikorel advertising	No breach	No appeal
385/1/96	Member of medical research ethics committee v Merck & Lipha	Acamprosate study alleged to be a marketing exercise	No breach	No appeal
386/1/96	Boehringer Mannheim v Boehringer Ingelheim	Promotion of Bonefos	No breach	Appeal by respondent
389/1/96	**Parke-Davis v Janssen-Cilag**	**Symposium report on topiramate (Topamax)**	**Breach 3.1, 7.2 & 7.4**	**No appeal**
390/1/96	**Consultant physician v Wyeth**	**Zoton press release**	**Breach 7.2**	**No appeal**
393/2/96	**Searle v Pfizer**	**Feldene Gel cost comparison**	**Breach 7.2**	**No appeal**
395/2/96 **405/2/96**	**Merck & Lipha & GP v Schering**	**Promotion of Progynova TS**	**Breach 7.2**	**No appeal**
396/2/96	**Organon v Novo Nordisk**	**Kliofem journal advertisement**	**Breach 7.2 & 7.3**	**No appeal**
397/2/96	**Hospital pharmacist v Dumex**	**Conduct of a representative**	**Breach 15.2**	**No appeal**

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 fifty 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 for promotional purposes
- the sponsorship of promotional meetings
- the sponsorship of scientific 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 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).