PRESCRIPTION MEDICINES
CODE OF PRACTICE AUTHORITY

CODE OF PRACTICE REVIEW

NUMBER 14 NOVEMBER 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.

Mountain bikes and gift vouchers

A recent case (AUTH/421/4/96 - reported in this issue of the Review) involved the offer of mountain bikes and Marks & Spencer's vouchers as inducements to buy medicines. This was ruled to be in breach of the Code by the Code of Practice Panel and this ruling was upheld by the Code of Practice Appeal Board. Norton Healthcare Limited failed to supply an adequate undertaking and the Appeal Board accordingly reported the company to the ABPI Board of Management.

Because of the possible ramifications of the decision, the ABPI subsequently took leading counsel's opinion on the outcome. Counsel expressed the view that the decision had been the correct one, though he commented that the relevant provision of the Code was somewhat obscure. A copy of the opinion has been sent to the Medicines Control Agency.

The ABPI Board asked the Authority to set up a working party to look at the relevant clause of the Code, Clause 18, and see whether it needed to be amended or to be made the subject of more detailed explanation and this is now in hand.

Norton Healthcare resigned from the ABPI as a consequence of the ruling and indicated that it would no longer accept the jurisdiction of the Authority. Any complaints which are received in the future about the company will be passed on to the Medicines Control Agency.

The Internet

Although no complaints have so far been received about material on the Internet, there have been many enquiries about it and a number of companies interested in putting material on the Internet, or in providing Internet facilities for other companies to use, have visited the Authority to discuss the matter.

An article on the Internet written by Heather Simmonds, the Authority's Secretary, appeared in the Code of Practice Review in May. As a consequence of that, Heather was invited by the United States' Food & Drugs Administration to attend a meeting in October to discuss the implications of putting promotional material and information about medicines on the Internet.

The position is under active consideration and further developments will be reported in the Review as they arise.

Complaints in 1996

By the end of October there had been 90 complaints in 1996. This compares with annual totals of 92 complaints in 1993, 145 in 1994 and 104 in 1995.

There has been an interesting change in the sources of complaints. In the years 1993, 1994 and 1995, 60-64% of complaints came from health professionals, mainly doctors and pharmacists, and 16-18% of complaints came from other pharmaceutical companies.

So far this year, however, slightly fewer complaints have come from health professionals than have come from companies. It remains to be seen what the position will be by the end of the year.

Membership of the Code of Practice Appeal Board

There are twelve industry members on the Code of Practice Appeal Board, all of whom must be senior executives in the industry and four of whom must be medically qualified. Membership of the Appeal Board involves a substantial commitment as the Appeal Board meets about ten times a year for a full day on each occasion and the reading of substantial paperwork is required in advance. Nonetheless, members of the Appeal Board find it to be an interesting and stimulating activity.

Vacancies arise from time to time and the Authority would be interested to hear from industry executives who feel that they are sufficiently widely experienced to be appointed and who are willing to devote adequate time to the activity.

Chalk and cheese advertising

A novel form of advertising which came before the Authority recently has been named "chalk and cheese" advertising after the imagery adopted. This form of advertising was where one company (Parke Davis & Company Limited) publicised breaches of the Code which had been ruled in relation to another company (Janssen-Cilag Limited). This was not the same as corrective advertising where a company is obliged to publish details of its own transgressions.

The two cases which involve such advertising are reported in this issue of the Review (Cases AUTH/442/7/96 and AUTH/444/7/96).

When considering complaints about the matter, the Code of Practice Panel considered that it was not in itself in breach of the Code to advertise in this way. This view was upheld by the Code of Practice Appeal Board upon appeal, but the Appeal Board was concerned at this type of advertising and suggested that it would be appropriate for the ABPI Board of Management to consider the principle. The ABPI Board decided that no action on its part was required at the present time. If this type of advertising became common, then the matter would have to be revisited.

Interactive data systems

Companies are reminded that the use of lap top computers and the like for promotional purposes is covered by the Code of Practice. Prescribing information must be provided in accordance with Clause 4.3 of the Code and the whole of the material on the computer must be certified in accordance with Clause 14.1.

Clause 14.1 requires that a written transcript of the material is certified including reproductions of any graphs, tables and the like that appear. In the event of a complaint being made, a copy of the written transcript would be requested.

Syndicate Leaders

Volunteers are sought to act on an occasional basis as syndicate leaders at the PMCPA seminars on the Code which are held at the Royal Society of Medicine in London.

There is no financial reward (though appropriate hospitality is provided!) but those taking on the role find it worthwhile and consider that it assists them in widening their knowledge of the Code.

If interested, please contact Jane Landles (0171-747 1415)

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, 17 January 1997
Thursday, 27 February 1997
Friday, 14 March 1997

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 Flynn at the PMCPA for details (0171-930 9677 extn 1443)

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 Flynn 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.

CASE AUTH/400/2/96

LEO v E MERCK

Curatoderm journal advertisement

Leo Pharmaceuticals complained about a Curatoderm advertisement issued by E Merck alleging that it was in breach of Clause 2 of the Code. There were four allegations and in addition a breach of Clause 2 of the Code was alleged.

The Panel ruled that a claim "Significant overall improvement was noted after just 2 weeks of therapy" had not been substantiated. Merck had submitted a pre publication manuscript marked "confidential" as part of the substantiation. This had not been considered by the Panel as claims had to be substantiated by data available to those who requested it. Merck appealed this ruling and in the circumstances the Appeal Board asked that the Panel reconsider the matter as it appeared that the consequences of marking data "confidential" had not be appreciated. Merck resubmitted data including an abstract of the manuscript; again the Panel did not consider that the limited amount of data supplied supported the strong efficacy claim. On appeal Merck submitted the full manuscript, no longer marked confidential, and said that it would have been made available to anyone who had not been satisfied with the abstract. The Appeal Board considered that the full manuscript did substantiate the claim and noted that Merck was willing to supply it. The circumstances were unusual but on the facts of this case no breach of the Code was ruled.

The Panel ruled that a claim "One application lasts from one night-time application to the next facilitating better compliance" was in breach of the Code as the comparator had not been made clear. This ruling was accepted by Merck.

A claim "All over treatment. Can be used all over the body even on the face and flexures" was considered by the Panel to be acceptable. Upon appeal by Leo the Appeal Board ruled that this claim was ambiguous in breach of the Code given that Curatoderm was not recommended for use on the scalp and it was not obvious whether the phrase "all over the body" included the scalp or not.

The Panel did not accept an allegation that the artwork was misleading with regard to the use of Curatoderm and exposure to sunlight. No breach of the Code was ruled.

The Panel ruled no breach of Clause 2 of the Code with regard to the advertisement as a whole.

Leo Pharmaceuticals complained about a journal advertisement for Curatoderm issued by E Merck Pharmaceuticals which appeared in GP, 16 February 1996. Leo alleged that the advertisement was in breach of Clauses 2, 7.2, 7.3 and 7.6 of the Code. The allegations were considered as follows:

1 Claim "EFFECTIVE Significant overall improvement was noted after just 2 weeks of therapy"

COMPLAINT

Leo provided the study referenced in the advertisement (Gerritsen *et al)* and pointed out that it was a placebo controlled right/left study which included efficacy in eight patients. There was no data relating to the comparison between tacalcitol (Curatoderm) and placebo after two weeks of treatment. Leo alleged that it was inappropriate to make any claim based only on the tacalcitol data without taking account of the placebo response. The company said it was it remarkable that these inadequate data were used to support this major claim.

INITIAL RESPONSE

Merck submitted that the claim was fair, accurate and balanced, based on an up-to-date evaluation of all the evidence and was capable of substantiation. The study referenced (Gerritsen *el al*) showed a very significant improvement in sum score at two weeks compared with baseline. Baseline comparisons were statistically valid especially under these conditions where placebo was known to have not only a placebo effect but acted as an emollient, which was one of the standard treatements for psoriasis. Further, Merck had unpublished data which supported the claim even more strongly than the reference cited. A manuscript was enclosed, which had been submitted for publication, giving the results of a larger placebo controlled right/left comparison study that clearly demonstrated a significant improvement with tacalcitol after just two weeks of therapy and for which the statistical calulation of probability compared with placebo was given ($p < 0.0001$). (Merck had marked this manuscript confidential and requested that it was not passed to Leo). Merck believed this data satisfied all the concerns raised by Leo.

INITIAL PANEL RULING

The Panel noted that the Gerritsen study referenced to support the claim was a placebo controlled double blind study using tacalcitol in only 10 patients with psoriasis vulagaris. Eight patients had been evaluated for efficacy and showed a marked clinical improvement. After two weeks of therapy both tacalcitol treated and placebo treated lesions showed significant improvement compared to baseline ($p \leq 0.001$ and $p \leq 0.03$ respectively). The Panel considered that a relevant factor was the difference between tacalcitol treatment and placebo treatment after two weeks therapy which would give information about the efficacy of the active ingredient and there was no data on this point in the study. The Panel therefore considered that the referenced study gave some support to the claim but was not sufficient to substantiate the claim. A cited reference did not, however, need to provide complete substantiation. It would be possible for additional material to the cited reference to be provided to substantiate the claim. Merck had provided a second study but had requested that it remain confidential and

that it not be shown to Leo. It could not therefore be taken into account. It the Panel's view, Clause 7.3 of the Code meant that claims had to be able to be substantiated by data which the company concerned was prepared to make available to enquirers. Given its criticisms of the cited study, the Panel decided that Merck had not substantiated the claim and therefore ruled a breach of Clause 7.3 of the Code.

INITIAL APPEAL BY MERCK

Merck understood that the finding of the Panel was not that the paper submitted was insufficient to substantiate their claim, but that this manuscript was not considered since it was marked confidential. Had Merck realised that this would be the case it would have submitted the same study data in a different form. The procedure and restrictions the Panel imposed on data supplied in response to a complaint was not clearly stated in the Code. Clause 7.4 required that substantiation must be provided at the request of members of the health professions which in Merck's view should be the test applied to data submitted to the Panel to substantiate material. The request that the information should not be made available to the complainant was not the same test as specified in Clause 7.4. The Constitution and Procedure stated that in such circumstances the matter would be referred to the Chairman of the Appeal Board. This did not occur. Merck said that if such a restriction was to be imposed on the use of supporting data then it should have been made aware of it at the time of its submission and it should be made clear in the Code.

Merck's reason for choosing to submit the manuscript to the Panel was merely to supply as full an account of the study as possible short of sending the full study report. The only reason for marking it confidential was because it had been submitted and accepted for publication and it would be unfair to the authors and the editors of the journal to make the full manuscript public prior to publication. None of the data contained in the manuscript was confidential. The study results had already been presented at a European Symposium. Merck enclosed a copy of the abstract from the symposium which they had been supplying to members of the health professions, where appropriate, in response to their enquiries. Further it had expanded upon the data contained in the abstract by supplying appropriate sections from the manuscript where necessary.

Merck asked that the Panel should reconsider the claim at issue with reference both to the abstract from the symposium and to the fact that Merck was willing to make available any item of information from the manuscript although it reserved the right to retain the confidentiality of the document in its entirety, until it had been published in an appropriate medical journal.

INITIAL APPEAL BOARD RULING

The Appeal Board considered that the implications of marking the manuscript confidential had not been appreciated by Merck and the consequences had not been explained to Merck prior to the Panel ruling on the matter. The problem had largely arisen as a result of the changes to Paragraph 7.2 of the Constitution and Procedure whereby, if a complaint was ruled no breach, then the complainant would be sent a copy of the comments and enclosures submitted by the respondent. The Appeal Board advised that the Authority should henceforth point out to respondents that, in cases alleging a failure to substantiate, the respondent should supply only substantiating material that would be available to any health professional asking for substantiation. This would hopefully avoid the problem in the case now before it.

Given the circumstances, the Appeal Board decided that the matter be remitted to the Panel for reconsideration. Merck should be contacted and asked to submit data to substantiate the claim in question. The information submitted must be that which was available at the time of the complaint and which could be supplied to any health professional (including those employed by pharmaceutical companies) requiring substantiation of the claim. In the event of no breach being ruled by the Panel, the substantiating information would be passed to Leo as required by the Constitution and Procedure.

Information was accordingly provided by Merck to the Panel which considered the matter afresh.

RESPONSE

Merck submitted that it had unpublished data which supported the claim even more strongly than the reference cited. This included the results of a study carried out involving 122 patients in a double-blind, placebo controlled, right-left comparison. The results of the study had been presented at a recent symposium and the abstract report from this symposium was provided. The results showed that two weeks after the start of treatment Curatoderm was significantly better than placebo ($p = < 0.0001$). Merck said that this data supported the claim.

PANEL RULING

The Panel noted its original criticisms of the Gerritsen study to which the claim was referenced and that the relevant factor would be the difference between tacalcitol treatment and placebo treatment after two weeks which would give information about the efficacy of the active ingredient and there was no data on this point in the study (see above).

The additional reference now provided by Merck to substantiate the claim was an abstract report from a symposium sponsored by Hermal and entitled "Tacalcitol (Curatoderm) - The New Vitamin D3 Derivative for the Topical Treatment of Psoriasis". The Panel noted that the Curatoderm trademark was owned by Hermal.

The Panel noted that to substantiate a claim it might not be adequate to only produce data in an abstract form. The information given in an abstract was selective and might not be sufficient to allow the reader to judge the original paper's quality or significance.

The Panel noted that the abstract did not include any actual results in detail. It merely stated that "The tacalcitol ointment was better than placebo regarding all criteria of efficacy. After only 2 weeks of treatment, symptoms such as reddening, infiltration, and scaling, as well as the sum of these measures, had shown significant improvements

($p < 0.0001$)". The abstract went on to say that after 8 weeks of treatment a clear additional improvement in the areas treated with tacalcitol could be seen in comparison to the placebo group. The Panel noted, however, that in the study efficacy was to be evaluated with regard to clinical symptoms such as redness, infiltration, scaling and itching as well as the size of the area affected and the global rating of physician and patient of the improvement of the skin. It appeared to the Panel that the only data after two weeks of treatment related to improvements in three parameters, reddening, infiltration and scaling as well as the sum of these measures which had shown significance ($p < 0.0001$). It was not clear whether this was an improvement compared to placebo or not. The Panel did not consider that improvement in only three parameters, as well as the sum of these measures could be regarded as overall improvement. The clinical significance of the changes was not stated.

The Panel considered that the abstract and the referenced study by Gerritsen did not provide adequate substantiation for the strong efficacy claim, "Significant overall improvement was noted after just 2 weeks of therapy". The Panel decided that Merck had not substantiated the claim and therefore ruled a breach of Clause 7.3 of the Code.

APPEAL BY MERCK

Merck provided the unpublished manuscript which had originally been put forward but which had been marked confidential and so had not been taken into account by the Panel in its original ruling.

Merck submitted that the manuscript clarified a number of points raised by the Panel. The sum score, which was a standard measure of treatment effect in psoriasis, was the primary efficacy criterion used in the study and therefore it was this parameter which determined whether the study was successful in showing a treatment effect or not. A highly significant difference between active and placebo treatment was seen after two weeks of treatment ($P < 0.0001$).

Merck noted that the manuscript was initially submitted to the Panel when the complaint was first made. Merck said that at the time it was asked to mark as "confidential", any document it did not wish to be passed on to Leo. The material had already been accepted by the British Journal of Dermatology (BJD) and therefore it owned the copyright. While normally the BJD was happy to allow release of such data to individuals in response to specific enquiries, it obviously did not permit any general publication of the material. It was only later that Merck was informed that the manuscript would be disregarded by the Panel if marked as confidential. Merck had not at that time therefore approached the BJD for permission to pass the manuscript on to Leo. Since the Panel judged the published abstract insufficient to support the claim when the matter was reconsidered by the Panel, Merck had sought permission from the BJD to pass on the manuscript to the Appeal Panel and to Leo but clearly required these data to be treated in the manner expected of a health professional making an enquiry ie it would be used solely for their own information.

Merck also enclosed a copy of the study summary from the clinical expert report which, provided a precis of the study findings.

APPEAL BOARD RULING

The Appeal Board noted that the letter from the Authority to Merck, advising it of the Appeal Board's decision to remit the case back to the Panel for reconsideration, had asked Merck to provide the material that it wished to put forward as substantiation for the claim in question and to confirm that all the information provided could be passed to Leo and would have been available to send to a health professional at the time the claim was made.

The Appeal Board agreed with the Panel that the data sent in response to that letter was not adequate to substantiate the strong efficacy claim. The Appeal Board questioned why the full manuscript had not been sent at that time. It was accepted, however, that requests to a company for information often resulted in a dialogue with the enquirer being sent concise information initially and more detailed and lengthy data if there was a further enquiry. The Appeal Board noted that the Merck had confirmed that if any enquirer, including a medical director from another pharmaceutical company, had not been satisfied with the abstract, at least the relevant parts of the manuscript would have been sent. The company also stated that a number of enquirers to the company's medical information department had been sent the abstract and had been satisfied.

The Appeal Board noted that material to substantiate a claim must be available to enquirers at the time the claim was made. Clause 7.4 of the Code stated that substantiation must be provided without delay. Material considered to be adequate to substantiate the claim should be sent in the first instance. While permission from the publishers to release the whole manuscript had only recently been requested by Merck, so that it could be sent to the Appeal Board for consideration, there was no evidence to suggest that Merck would not have sought such permission earlier in response to a request. The Appeal Board considered that the full manuscript did substantiate the claim "Effective significant overall improvement was noted after just 2 weeks of therapy" and that Merck was willing to supply it on request. The Appeal Board noted that the circumstances were somewhat unusual but on the facts of this case ruled that there was no breach of Clause 7.3 of the Code.

The appeal was therefore successful.

2 Claim "One application lasts from one night-time application to the next, facilitating better compliance"

COMPLAINT

Leo alleged that the phrase "facilitating better compliance" was a hanging comparison.

RESPONSE

Merck accepted that the claim included a hanging comparison because of the use of the comparative adjective "better". This was an oversight and would be corrected.

RULING

The Panel noted that the implication was that compliance with Curatoderm would be better than compliance with other treatments. The Panel ruled a breach of Clause 7.2 of the Code as the comparator had not been made clear.

3 Claim "ALL OVER TREATMENT Can be used all over the body even on the face and flexures"

COMPLAINT

Leo pointed out that the prescribing information clearly stated that Curatoderm was not recommended for use on the scalp. Curatoderm could not, therefore, be considered to be an "all over treatment" for patients with psoriasis vulgaris. In addition the claim suggested that the whole body could be treated with Curatoderm. This was grossly misleading in view of the clear statement within the prescribing information that the amount applied should not exceed 5g ointment per day. This amount was clearly insufficient to provide "all over treatment".

RESPONSE

Merck said that the prescribing information, which formed part of the advertisement, clearly stated that Curatoderm was not recommended for use on the scalp. It was not usual practice to repeat all the restrictions for a product beyond the prescribing information. Further, it was well recognised and understood by all health professionals that ointments were not suitable for the scalp and therefore it was unnecessary to repeat this.

Similarly, it was quite clearly stated in the prescribing information that the maximum daily dose of Curatoderm was 5g. Merck did not intend to imply that the whole surface of the body could be treated with the tacalcitol at the same time. Clinicians were aware that such treatments were only applied to the lesions. Further they were aware that the difficult to treat and often restricted areas were the face and flexures. The use of "even on the face and flexures", made clear that the use of Curatoderm was not restricted in these difficult areas. Merck was confident that health professionals who were involved in the treatment of psoriasis would readily interpret its statement in the way it was intended.

PANEL RULING

The Panel noted that the summary of product characteristics (SPC) included the statement that "Curatoderm is not recommended for use on the scalp". This also appeared in the prescribing information in the advertisement.

The Panel accepted the submission that health professionals recognised and understood that ointments were not generally suitable for the scalp. In the Panel's view, doctors would assume that an ointment was unsuitable for application to the scalp unless otherwise advised. The Panel might have had a different view if Curatoderm was available as a cream, gel or a lotion which were more suitable for scalp application. In addition, general usage of the word "body" would be taken to mean everything except the scalp.

The Panel did not accept that the phrase "all over treatment..." would mislead doctors into thinking that Curatoderm was to be applied all over the body when used. Psoriasis was a familiar condition in general practice and doctors would be aware that topical antipsoriatics were applied only to affected lesions. It would be most unusual to do otherwise.

The Panel ruled no breach of Clause 7.2 of the Code.

APPEAL BY LEO

Leo did not accept that general usage of the word "body" would be taken to mean everything except the scalp. Members of the medical profession would undoubtedly include the scalp within the totality of the body. It was well known within the medical profession that approximately 50% of patients presenting with psoriasis had scalp involvement. Within this context, therefore, the claim "all over treatment" would lead the prescriber to believe that Curatoderm was suitable for scalp application. In addition the phrase "even on face and flexures" emphasised the claim for universal application.

Leo said that it was wrong to think that doctors would assume that an ointment was unsuitable for application to the scalp. A number of scalp applications were marketed in the UK: Cocois Ointment, Lenium Cream, Pragmatar Cream, Psoriadrate Cream. Other applications such as Calmurid Cream were also commonly used on the scalp. Furthermore, Leo's research in January 1994, prior to the launch of Dovonex Scalp Solution, found in a survey of 180 general practitioners and 53 dermatologists that 25-27% were prescribing Dovonex as cream or ointment, but predominantly ointment, for scalp treatment.

Leo also said that it was wrong for the Panel to place great importance on an assumption that "an ointment was unsuitable for application to the scalp unless otherwise advised". The claims "all over treatment - can be used all over the body" advised doctors to use Curatoderm in a general anatomical distribution which included the scalp. The fact that the SPC and prescribing information included the statement that Curatoderm was not recommended for use on the scalp was irrelevant. It was unacceptable to rely on a contraindication within the prescribing information to balance a major claim of this nature.

RESPONSE BY MERCK

Merck submitted that the claim would not be taken to include the scalp. In common English usage, and in medical usage, the parts of the anatomy included in the term "body" varied depending on the context. In relation to the application of a medicinal or cosmetic product there appeared to be a clear understanding of separate reference to the body and head (or scalp). The fact that this debate was occurring at all demonstrated that the contention by Leo that "the medical profession would undoubtedly include the scalp as within the totality of the body" was wrong. The statement in the advertisement was quite clearly focusing on treatment of the face and flexures - areas that were traditionally difficult to treat because of the limited options available.

Merck was certain that doctors would assume that an ointment was unsuitable for application to the scalp

unless otherwise advised. Leo noted that approximately 50% of patients presenting with psoriasis had scalp involvement. Despite this, and considering the major breakthrough that calcipotriol provided in the treatment of psoriasis, 75% of doctors had not attempted to use any of the preparations then available to treat scalp psoriasis. Leo stated that only a quarter of doctors had used either a cream or ointment for the treatment of scalp psoriasis. As the data did not state the percentage using ointment it might perhaps be assumed that the proportion using ointment was unimpressive. Merck submitted that the findings only emphasised the poor suitability of ointments for use on the scalp and in particular, while a specific calcipotriol scalp solution was available and promoted, prescribers would be unlikely to use Curatoderm ointment to treat psoriasis on the scalp.

Further testimony to the lack of suitabilty of ointments for treatment of the scalp was demonstrated by the production of specific scalp solutions. The list of scalp solutions marketed in the UK provided by Leo cited products which were specifically indicated for the scalp and met the exceptions noted by the Panel that doctors would assume that an ointment was unsuitable for application to the scalp unless otherwise advised. Assessment of the BNF for topical psoriasis treatments clearly differentiated between ointments (for use on the skin) and products specifically developed for the scalp or the skin and scalp. The only ointment listed for use on the scalp was Cocois Scalp Ointment. This product was specifically designed as a scalp preparation and was described as such in its name therefore more than satisfying the exception described by the Panel.

Merck submitted that the prescribing information which stated that Curatoderm was not recommended for use on the scalp formed a very important part of the advertisement and its contents could not be ignored. No claim had been made for use of Curatoderm on the scalp. The SPC stated that "Curatoderm is not recommended for use on the scalp" in the section headed "Special warnings and precautions for use" and not in the section headed "Contra-indications". The company did not have the data for use on the scalp.

FURTHER COMMENTS FROM LEO

Leo maintained that if the face was to be included in the all embracing statment "all over the body" then there was a clear indication that the scalp could also be treated. On which part of the body was the face to be found? The Curatoderm advertisement clearly showed a female face on the front of a head, below the scalp. The "body" was not shown! Where the face ends and the scalp begins was commonly affected in psoriasis - a point well known to Merck.

Leo reemphasised that it was common practice among dermatologists and GPs to prescribe ointments and creams for application to the scalp.

Leo said that the claim was clearly intended to emphasis a lack of any restriction on the usage of the product. The restriction within the text of the prescribing information did not balance the claim sufficiently.

APPEAL BOARD RULING

The Appeal Board noted that the scalp was an area that was particularly affected by psoriasis. Curatoderm was not recommended for use on the scalp. It would be unacceptable for Merck to promote Curatoderm for use on the scalp. The advertisement was silent on the point and only mentioned in the prescribing information that Curatoderm was not recommended for use on the scalp. Similarly there was no mention in the main body of the advertisement that Curatoderm was an ointment. That information only appeared in the prescribing information.

The Appeal Board considered that the claim "All over treatment. Can be used all over the body - even on the face and flexures" was ambiguous given that Curatoderm was not recommended for use on the scalp and that it was not obvious whether the phrase "all over the body" included the scalp or not. The Appeal Board therefore ruled a breach of Clause 7.2 of the Code.

The appeal on this point was successful.

4 Artwork

The illustration in the advertisement was of a female with closed eyes. One eye had been painted over with a sun and the other with a moon and stars. The most prominent display of the brand name Curatoderm had the capital letter "O" coloured orange and the capital letter "D" was half coloured blue with the other half coloured orange.

COMPLAINT

Leo alleged that the artwork was misleading. The artwork associated tacalcitol treatment with sunlight and the inclusion of a "sun logo" within the trade name would immediately suggest that exposure to sunlight was not only acceptable but beneficial used together with tacalcitol. The SPC clearly stated that when patients were to be exposed to sunlight, tacalcitol should be applied at bedtime and also that sunlight might degrade tacalcitol.

RESPONSE

Merck said that the image was designed to convey the message of once daily application - which lasted through the day and night. The background of the image with the warm colour scheme suggested sunset and reinforced Merck's suggestion for nighttime application.

The Curatoderm logo quite clearly highlighted o.d. This was standard nomenclature for once daily and reinforced the message of the face image to suggest once daily application by forming a link with the sun and moon and once daily.

Merck's market research, using general practitioner subjects, showed that this image was interpreted as supporting the idea of the dosage regime. There was no suggestion of sunlight being a part of the treatment.

While ultra violet (UV) light might degrade tacalcitol, Merck did not advocate that sunlight should be avoided when using the product - far from it, for most psoriasis sufferers sunlight was a beneficial adjunct to treatment. The SPC mentioned the use of tacalcitol in combination with UV therapy. It was clear from the SPC that night-time

application of tacalcitol was all that was required if exposure to sunlight was anticipated.

RULING

The Panel noted that the SPC stated that "When patients are likely to be exposed to sunlight, tacalcitol should be applied at bedtime" and that UV light including sunlight may degrade tacalcitol.

The Panel did not accept that the artwork was misleading as alleged given the statements in the SPC and the response from Merck. The Panel therefore ruled no breach of Clause 7.6 of the Code.

5 Alleged breach of Clause 2

COMPLAINT

Leo alleged that this kind of promotional activity brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was alleged.

RESPONSE

Merck submitted that Clause 2 related to very serious matters. The error made regarding the hanging comparison (point 2 above) was not sufficient to invoke a breach of Clause 2.

RULING

The Panel did not accept that the advertisement as a whole 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.

Complaint received **14 February 1996**

Case completed **10 July 1996**

CASE AUTH/416/3/96

LUNDBECK v LILLY

Prozac leavepiece

Lundbeck complained about a Prozac leavepiece issued by Lilly. It was alleged that the statements "No clinically significant interactions have been reported when Prozac is used in combination with the following drugs in common use: Analgesics, Sedatives, Antibiotics, Antacids, Antihistamines, Diuretics, H2 blockers, Antihypertensive agents, Oral contraceptives" and "Despite a high level of protein binding, no clinically significant interactions between Prozac and warfarin, chlorothiazide, tolbutamide or diazepam have been reported" failed to provide an accurate presentation of the available evidence. The published literature documented important interactions. The statement that "So Prozac is a suitable treatment for patients on other medications, including those commonly used in the elderly" was alleged to be all embracing and misleading.

The Panel considered that the leavepiece was misleading as it understated the position as to possible interactions. No account had been taken of the contraindications and warnings in the data sheet and the papers referred to by Lundbeck cast doubt on the statements made in the leavepiece. Breaches of the Code were ruled and these rulings were upheld on appeal by Lilly. The Appeal Board was concerned that the leavepiece gave the impression that Prozac could be safely co-administered with all other medicines.

Lundbeck Limited complained about a leavepiece issued by Lilly Industries Limited in relation to Prozac (reference number PZ694A). The Prozac leavepiece in question had been passed to psychiatrists and hospital pharmacists by Lilly's Psychiatric Specialist Representatives and Technical Pharmacists when clarification of interaction issues was needed. There were two allegations.

1 Interactions

COMPLAINT

Lundbeck said that on the second page of the item the following statements were made:

"No clinically significant interactions have been reported when Prozac is used in combination with the following drugs in common use: Analgesics, Sedatives, Antibiotics, Antacids, Antihistamines, Diuretics, H_2 blockers, Antihypertensive agents, Oral contraceptives".

and

"Despite a high level of protein binding, no clinically significant interactions between Prozac and warfarin, chlorothiazide, tolbutamide or diazepam have been reported".

Lundbeck said that published literature clearly documented important interactions reported to have occurred among patients receiving fluoxetine:

Warfarin Woolfrey et al (British Medical Journal) and Hanger Thomas (New Zealand Medical Journal) each reported two cases of loss of anticoagulant control.

Clarithromycin (antibiotic) Pollak et al (Annals of Pharmacotherapy) reported a case of acute confusional disorder;

Pentazocine (analgesic) Hansen et al (American Journal of Psychiatry) reported an excitatory interaction;

Chloral hydrate (sedative) Devarajan (Canadian Journal of Psychiatry) reported prolonged drowsiness;

Terfenadine (antihistamine) Swims (Annals of Pharmacotherapy) reported sinus tachychardia;

Cyproheptadine (antihistamine) Katz & Rosenthal (Journal of Clinical Psychiatry) reported a return of depressive symptoms.

Both claims failed to provide an accurate presentation of the available evidence and were alleged to be in breach of Clause 7.2.

RESPONSE

Lilly said that this allegation challenged statements regarding the lack of clinically significant interactions between Prozac and analgesics, sedatives, antibiotics, and antihistamines, and more specifically between Prozac and warfarin.

The product data sheet represented the most up-to-date and complete evaluation of interaction data available, based on a database of clinical trial data and both reported and ongoing evaluation of adverse event reports. The promotional material should reflect the content of the current product data sheet which was last reviewed in February 1996.

Lilly said that the statements in the leavepiece were clearly presented and entirely consistent with the Prozac licence, which represented the most accurate summary of the evidence available to Lilly. The case reports cited did not in isolation add to Lilly's current knowledge of adverse events associated with Prozac, but Lilly would of course continue to assess their clinical significance in the light of any future reports, and amend the data sheet and any promotional material subsequently if appropriate. Detailed comments were as follows:

Warfarin Attention was drawn to two publications (Woolfrey et al, BMJ; and Hanger and Thomas, NZMJ), each describing two cases where there was a temporal association between the use of Prozac and loss of anticoagulant control in patients previously stable on warfarin. It was difficult to infer causality from these cases. Lilly's own animal and healthy volunteer data showed no evidence of a clinically significant interaction with warfarin. This was backed up by a study of seven patients, well controlled on warfarin, who showed no significant change in prothrombin times ratio on addition of Prozac 20mg daily (Ford et al, Pharm Sci Comm). In addition, spontaneous reports of possible warfarin interactions had been extremely rare, particularly when viewed in the light of the large number of patient exposures to Prozac.

Weighing up the available evidence, Lilly was therefore forced to question the clinical significance of the four case reports referred to in the complaint, and did not feel that they rendered the statement in the leavepiece regarding interactions with warfarin, which was entirely consistent with the current data sheet, false or misleading.

Clarithromycin The complaint refered to an isolated case report of organic psychosis in a patient taking Prozac 80mg (a dose outside the UK licence for depression) and nitrazepam 10mg daily, who was commenced on clarithromycin for a respiratory infection (Pollak et al, Annals Pharmacother). The authors constructed a theoretical argument proposing that accumulation of fluoxetine following an interaction with clarithromycin in the cytochrome P450 hepatic enzyme system was one possible explanation for the symptoms experienced. Actual drug levels were not reported, however, and the possibilities of an interaction between nitrazepam and clarithromycin, or of a toxic psychosis secondary to infection, were dismissed.

Despite a general statement in the Prozac data sheet alerting the reader to the theoretical possibility of interactions between Prozac and drugs whose metabolism involved the cytochrome P450 system, Lilly did not consider that this case report presented sufficient evidence to render the general statement made in the leavepiece regarding interaction with antibiotics, which was entirely consistent with the current data sheet, false or misleading.

Pentazocine Hansen et al (Am J Psych) reported an isolated case of transient lightheadedness, anxiety, nausea, paraethesiae, sweating, flushing, ataxia, mild tremor and hypertension on first exposure to pentazocine in a patient on 40 mg Prozac daily. The authors themselves noted that given the patient's single exposure to the combination, and lack of previous exposure to pentazocine, it was possible that the symptoms were due to pentazocine alone, and thus it was impossible to confidently ascribe causality to a putative interaction. Lightheadedness, nausea, sweating, flushing, tremor and hypertension were all listed as reported adverse effects in the pentazocine data sheet (Sanofi Winthrop, 1995-6). The authors' invitation for further reports of a similar nature did not appear to have been taken up with enthusiasm, and Lilly was aware of no such reports.

The isolated report did not contradict the statement in the leavepiece regarding the lack of clinically significant interactions between Prozac and analgesics which was entirely consistent with the current data sheet.

Chloral hydrate Devarajan (Can J Psych) reported a single isolated case of moderate but prolonged drowsiness in a patient taking Prozac 20mg daily and subsequently administered chloral hydrate. Again, causality was difficult to ascribe since drowsiness was the primary CNS effect of chloral hydrate and there was no information on previous exposure of the patient to chloral hydrate without Prozac. Both Prozac and chloral hydrate were protein bound and the possibility existed that plasma concentrations might be altered by their concomitant administration. Lilly knew of no other reported cases, however, and it was worth noting that formal studies of other protein bound drugs such as chlorothiazide, ethanol, secobarbital and tolbutamide had not shown clinically significant interactions with Prozac.

This isolated report did not contradict the statement in the leavepiece regarding the lack of clinically significant interactions between Prozac and sedatives which was entirely consistent with the current data sheet.

Terfenadine Swims (Annals Pharmacother) reported a single isolated case of intermittent sinus tachycardia in a patient taking fluoxetine, terfenadine, ibuprofen, misoprostol. acetaminophen, dichloralphenazone, isometheptene and ranitidine. The author, in her own words, "speculated" that the cardiac abnormalities reported were attributable to the inhibition of the metabolism of terfenadine by Prozac. Again causality had not been established satisfactorily in this report where there were multiple concomitant medications. Lilly knew of no other similar reports. Lilly did not consider that

speculation had any part to play in pharmacovigilance.

This isolated report did not contradict the statement in the leavepiece regarding the lack of clinically significant interactions between Prozac and antihistamines which was entirely consistent with the current data sheet.

Cyproheptadine Katz & Rosenthal (J Clin Psych) reported a single isolated case of recurrence of depressive symptoms in a patient treated with cyproheptadine following successful treatment of depression with Prozac 40mg (a dose outside the UK licence for depression). Despite the weight the authors lent to the patient's own report of a self-initiated and self-monitored re-challenge and recurrence, Lilly did not feel that this report comprised clear evidence of an interaction. In contrast, a paper by McCormick et al (J Clin Psych) described the use of cyproheptadine in the treatment of fluoxetine-induced anorgasmia without recurrence of depressive symptoms.

This isolated report did not contradict the statement in the leavepiece regarding the lack of clinically significant interactions between Prozac and antihistamines which was entirely consistent with the current data sheet.

PANEL RULING

The Panel accepted that it was arguable as to the clinical significance of the reported interactions referred to by the complainant but considered that their existence cast doubt on the veracity of the statement made that "No clinically significant interactions have been reported when Prozac is used in combination with the following drugs in common use: Analgesics, Sedatives, Antibiotics, Antacids, Antihistamines, Diuretics, H_2 blockers, Antihypertensive agents, Oral contraceptives".

In relation to the statement "Despite a high level of protein-binding, no clinically significant interactions between Prozac and warfarin, chlorathiazide, tolbutamide or diazepam have been reported", the Panel noted that there could be considerable debate over the clinical significance of spontaneous reports. The Prozac data sheet said that "In formal testing, no drug interaction of clinical significance has been observed between fluoxetine and warfarin. Possible interactions have been reported rarely". The Panel noted that it was generally accepted that "formal testing" could not completely exclude the possibility of a drug interaction. The Panel considered that it was not acceptable to dismiss totally the reference in the data sheet to interactions with warfarin and the four published cases and to claim that "no clinically significant interactions ..... have been reported".

The Panel considered that the leavepiece understated the position as to possible interactions and was misleading in that regard. The Panel therefore ruled a breach of Clause 7.2 of the Code.

APPEAL BY LILLY

Lilly said that it was important to clarify more formally the clinical significance of isolated case reports versus data gathered in formal interaction testing and where regulatory authorities had not deemed it necessary to add these to data sheets.

Lilly submitted the following additional arguments on specific drug interactions.

Warfarin The clinical significance implied manifestations of clinical signs or symptoms. The two publications described only changes in laboratory values, but did not mention medically significant adverse events resulting from those changes.

Pentazocine The metabolising isoenzyme was most likely 1A2 (Ciraulo et al, 1995). This paper referred to increased metabolism of pentazocine in smokers. This was secondary to induction of 1A2 by nicotine, the only isoenzyme activated by nicotine. There were no data on metabolism through the same pathway as fluoxetine (2D6). The case presented by Hanson of the signs and symptoms manifested by the patient were clinically significant. Lilly also believed that they were due to pentazocine alone because of the high dose (100mg).

Terfenadine / clarithromycin Lilly did *in vivo* and *in vitro* studies that involved 3A4 isoenzyme, and found no clinically significant interactions between fluoxetine and terfenadine (a study summary report was supplied). Since clarithromycin was metabolised through the same pathway, no clinically significant interactions would be expected.

Chloral hydrate This was metabolised in the liver, like ethanol (alcohol dehydrogenase). There was no interaction between fluoxetine and alcohol, thus no interaction with chloral hydrate would be expected (Schaffler, 1986, Lemberger et al 1985). Neither chloral hydrate, nor its active metabolite were highly bound to plasma proteins. Therefore, this mechanism of interaction seemed to be improbable.

Cyproheptadine Due to the anti-serotonergic mechanism of action of cyproheptadine, the recurrence of depressive symptoms was an example of pharmacological antagonism and not interaction.

APPEAL BOARD RULING

The Appeal Board agreed with the Panel's view that the two statements in question were unacceptable in the light of the reported interactions referred to by the complainant. Care had to be taken with the word "reported" in relation to interactions. An interaction could have been "reported" even if it had not been definitively established. The papers referred to by the complainant cast doubt on the statements made in the leavepiece. Further, the data sheet for Prozac stated in relation to interactions with warfarin that "Possible interactions had been reported rarely". The Appeal Board upheld the Panel's ruling that the leavepiece was misleading in breach of Clause 7.2. The appeal on this point therefore failed.

2 Contraindications and precautions re use of Prozac.

COMPLAINT

Lundbeck said that the prescribing information and data sheet clearly documented that fluoxetine was contraindicated for use with MAOIs (monoamine oxidase inhibitors). Caution was also advised with co-administration of fluoxetine and tryptophan or CNS active drugs, including lithium. It was also recommended

that concomitant treatment with drugs predominantly metabolised by the hepatic cytochrome P450IID6 isoenzyme system and which had a narrow therapeutic index (eg, flecainide, carbamazepine and tricyclic antidepressants) be initiated at or adjusted to the lower end of the dose range. An interaction with phenytoin was also described.

Lundbeck alleged that the statement in the leavepiece that "So Prozac is a suitable treatment for patients on other medications, including those used commonly in the elderly" was all embracing and misleading and in breach of Clauses 7.2 and 7.8.

RESPONSE

Lilly said that the term "suitable treatment" implied adequacy, rather than perfection, and certainly did not imply universal safety in use. Administering a "suitable treatment" did not preclude the exercising of reasonable cautionary measures with concomitant medications, such as those outlined in the data sheet. The statement referred to did not state or imply that Prozac was a suitable treatment for ALL patients on other medications. Indeed, taken within the context of the information contained on the same page of the leavepiece, the statement clearly referred to the medications listed on that page.

PANEL RULING

The Panel considered that the statement "So Prozac is a suitable treatment for patients on other medications, including those used commonly in the elderly" was misleading for similar reasons of understatement as in point 1 above. No account had been taken of the contraindications and warnings in the prescribing information and/or data sheet. This statement also was ruled to be misleading in breach of Clause 7.2.

APPEAL BY LILLY

Lilly said that it was interesting to note that the complainant's view was based primarily on the role of cytochrome P450 within the metabolism of other drugs. Again, the same argument as previously iterated in point 1 above and also in Lilly's original correspondence should be considered.

In addition, in response to Lundbeck's comment regarding the cytochrome P450IID6 isoenzyme system, most data related to *in vitro* work or individual metabolism of products rather than direct interaction studies. Extrapolations had been drawn from the laboratory which had not been borne out by what had been seen in the course of pharmacovigilance.

While Lilly recognised that there were some specific contraindications of monoamine oxidase inhibitors and also caution with regard to tryptophan or lithium, these were not used commonly in the elderly. Similarly co-administration of tricyclic antidepressants with a selective serotonin reuptake inhibitor would not be routine practice. Lilly submitted that its statement would not be seen to be a breach of the Code.

APPEAL BOARD RULING

The Appeal Board agreed with the Panel that the statement "Prozac is a suitable treatment for patients on other medications, including those used commonly in the elderly" was misleading as it took no account of the contraindications and interactions referred to in the prescribing information and the data sheet. The British National Formulary also referred to interactions. The Appeal Board considered that the statement bordered on the irresponsible given that another page listed a number of medicines where care was needed when taken concurrently with Prozac. The Appeal Board upheld the Panel's ruling of a breach of Clause 7.2 of the Code. The appeal on this point therefore failed.

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In the light of the above rulings the Appeal Board expressed serious concern that the leavepiece gave the impression that Prozac could be safely co-administered with all other medicines and asked that its concern be conveyed to Lilly. The Appeal Board also asked that Lilly be told of its concern that the qualifying statement "Prozac is contra-indicated for use with MAOIs. Caution is advised with co-administration of Prozac and tryptophan or CNS drugs, including lithium" had been printed as a footnote in a very small type size.

Complaint received **29 March 1996**

Case completed **15 August 1996**

CASE AUTH/421/4/96

DIRECTOR/SCRUTINY v NORTON HEALTHCARE

Journal advertisement for prescription only medicines - inducements to purchase

An advertisement for certain prescription only medicines issued in association with Norton Healthcare was taken up during the routine scrutiny of journal advertisements. The advertisement offered Marks & Spencer's vouchers and/or a mountain bike when purchasing certain prescription only medicines. As the matter could not be settled it was referred to the Panel as a case.

The Panel ruled that the offer of Marks & Spencer's vouchers and mountain bikes was an inducement to health professionals to purchase prescription medicines. A breach of the Code was ruled. This ruling upheld by the Appeal Board on appeal by Norton Healthcare.

This case arose from the routine scrutiny of journal advertisements. As the matter could not be settled, it was referred to the Code of Practice Panel as a case in accordance with Paragraph 17.4 of the Constitution and Procedure.

The advertisement in question, published in Chemist & Druggist 23 March 1996, referred to "POM deals for Haycrom 13.5 ml, terfenadine 60 mg, loperamide 2 mg and terfenadine forte 120 mg." The advertisement was headed "Europharm Eurochem Cavendish in association with Norton Healthcare". A number of offers to purchasers when spending "across the range" were mentioned in the advertisement. For example "£900 and receive £90 M & S vouchers - 1 mountain bike and £10 M & S voucher".

COMPLAINT

In the Authority's view, as Haycrom 13.5 ml was a prescription only medicine (POM) and certain quantities of loperamide and terfenadine were also POMs, the advertisement came within the scope of the Code. It was pointed out to Norton Healthcare Limited that the advertisement was in breach of Clause 18.1 of the Code as it offered unacceptable inducements in the form of Marks & Spencer's vouchers and mountain bikes to purchasers of medicines.

RESPONSE

Norton Healthcare submitted that the advertisement fell outside the scope of the Code as defined in Clause 18.1. The supplementary information to Clause 18.1 exempted measures or trade practices relating to prices, margins and discounts, which were in existence in the pharmaceutical industry on 1 January 1993. Norton Healthcare was of the opinion that Europharm was repeating a trade practice that was in existence prior to 1 January 1993. By way of example, Norton Healthcare supplied details of a promotional scheme operated by a named pharmaceutical company in 1990 and later, whereby retail pharmacy discounts were offered in the form of Argos vouchers. A similar scene was run by another pharmaceutical company whereby retail pharmacies could earn air miles on orders received. Norton Healthcare submitted that these were two of many such examples which, in line with the Europharm scheme in question, offered discounts of similar value to more traditional discounting methods such as straight price discounts or free stock.

PANEL RULING

The Panel noted that there had been a number of changes to the Code in relation to trade practices and the like over recent years. The Code reflected the requirements of The Medicines (Advertising) Regulations 1994 (SI 1994 No 1932) and the EC Council Directive on the advertising of medicinal products for human use in relation to both the exemption of certain trade practices and the provision of gifts, benefits in kind or pecuniary advantages.

The Panel noted that measures or trade practices relating to prices, margins or discounts which were in existence in the pharmaceutical industry on 1 January 1993, were exempt from the Code (Clause 1.2). The 1994 edition of the Code had been similarly worded apart from the phrase "in the pharmaceutical industry" which had been introduced in the 1996 edition of the Code.

The Panel noted that a complaint about a similar scheme to the one in question had been recently received from the Medicines Control Agency (MCA). The company concerned, a dental company, was not a member of the ABPI and had declined to comply with the Code and accept the jurisdiction of the Authority. The matter had therefore been referred back to the MCA which was currently taking action.

The Panel noted that the advertisement mentioned Europharm, Eurochem and Cavendish and contact numbers were included for these three companies which were understood to be wholesalers. The Panel noted that Norton's submission referred to the scheme as the Europharm scheme. The Panel considered that Norton was party to the scheme as the advertisement stated "in association with Norton Healthcare". Wholesalers themselves were not directly subject to the ABPI Code as it only applied to pharmaceutical companies. In the Panel's view, however, the advertising regulations would apply to wholesalers.

The Panel did not accept that the provision of Marks & Spencer's vouchers and/or mountain bikes in association with sales of prescription medicines was a trade practice exempt from the requirements of the Code as it did not relate to prices, margins or discounts. The Panel accepted that similar schemes to the one in question might well have been in existence before 1 January 1993 but as the scheme in question did not relate to prices, margins or discounts, it was not exempt from the Code. The Argos voucher and air miles schemes used as examples by Norton Healthcare might at one time have been acceptable in relation to the requirements of the Code. The Code was now more restrictive in relation to trade practices and the like.

The Panel noted the requirements of Clause 18.1 of the

Code that no gift, benefit in kind or pecuniary advantage shall be offered or given to members of the health professions or to administrative staff as an inducement to prescribe, supply, administer or buy any medicine, subject to the provisions of Clause 18.2.

The provision of Marks & Spencer's vouchers or mountain bikes could not be considered to come within Clause 18.2, which covered promotional aids which were limited in cost to no more than £5 and had to be relevant to the practice of the recipient's profession.

The Panel considered that Marks & Spencer's vouchers and mountain bikes were personal benefits not related in any way to the practice of medicine or pharmacy. The offer of Marks & Spencer's vouchers and mountain bikes in the advertisement was an inducement to health professionals to purchase prescription only medicines. The Panel therefore ruled that Norton Healthcare was in breach of Clause 18.1 of the Code.

APPEAL BY NORTON HEALTHCARE

Norton Healthcare submitted that the advertisement in question was placed by Europharm, Eurochem, Cavendish and carried the wording "In association with Norton Healthcare" as products offered were from the range made by Norton. As such Norton was not responsible for the drafting or approval of the advertisement. The company pointed out that perhaps the most straightforward resolution to the issue would be for Norton to direct that Europharm removed any reference to its company from the advertisement. Such action would however avoid a debate and more serious consideration of what Norton deemed to be an acceptable means of promotion and furthermore a means of promotion that was allowed under the Code.

Norton did not accept that the offer of the vouchers or a mountain bike constituted a gift, since the implicit meaning of "gift" was a donation without preconditions. Clearly the goods were offered as a direct consequence against the qualifying purchases and as such were equivalent to a discount. Goods were offered instead of cash. Indeed the discount that these items would equate to was about 10% which was far less a discount than many other companies were using to induce pharmacists to stock or use their products. The pharmacist in many cases could buy two or four times the number of Marks & Spencer's vouchers or mountain bikes with the discount offered by other companies.

Norton accepted that the offer of vouchers or mountain bikes could be considered a benefit in kind to the extent that both had cash values. Equally however the offer of price discounts, free stock etc could also be regarded as benefits in kind and if so subject to Clause 18. Yet the Panel would be aware that pharmaceutical companies had offered, and continued to offer, a wide variety of discounts on pharmaceutical purchases. Norton submitted that one should ask whether a pecuniary advantage was being offered in the transaction and whether there was some monetary or fiscal advantage or some other advantage pertaining to money being offered in the transaction. The answer to this point was also yes but then equally discounts and free stock offers would also constitute pecuniary advantages.

Norton was surprised and could not accept the Panel's opinion to the effect that the scheme was anything other than a manifestation of a trade practice outside the scope of the Code under the supplementary information to Clause 18.1 which exempted "Measures or trade practices relating to prices, margins and discounts which were in existence in the pharmaceutical industry on 1 January 1993".

The company referred to another advertisement issued by Europharm, Eurochem, Cavendish in association with another pharmaceutical company which offered CD or record vouchers or a mountain bike with purchases of certain POMs.

The company referred to a number of examples of promotional schemes offered or currently on offer as mentioned in its submission to the Panel. The company also drew attention to a scheme operated by a pharmaceutical company in which one point was awarded for every £50 worth of qualifying sales of prescription only medicines. Points collected could be redeemed at high street retailing groups. Another company also operated a scheme in 1991 where vouchers for goods were offered against product purchases to participating retailers. This scheme was still in operation today. Similarly another company was known to have operated a scheme before 1 January 1993 in which prescription medicines purchasers received credit allocation and these credits could be redeemed for gifts from the brochure accompanying the scheme. The company submitted that there was *prima facie* evidence that the effects of the trade practice in question predated 1 January 1993 and therefore equivalent schemes should be allowed under the Code.

Norton said that the Panel's observation that the scheme in question did not relate to prices, margins or discounts was illogical. By inference it would appear that the Panel was suggesting that the offer of such goods was not related to prices, margins or discounts. Norton reiterrated its belief that the scheme was a trade practice relating to these points. The company did not regard there to be any fundamental distinction between the offer of goods (including free stock) and price discounts or margin allowances or cash back (for example retrospective rebates) all of which were ubiquitous methods of promotion in the pharmaceutical industry. They all had in common one factor, that was, a monetary value. In general when such schemes were more closely inspected it could be seen that the greater monetary value to the purchaser was often free stock offering. What should not be in dispute was that all these forms of promotion had a cash value to the purchaser, whether they be independent retail pharmacists, small multiples or bodies corporate. The company did not accept that there was a facility within the Code to distinguish between these forms of promotion particularly since they were all in existence before and after 1 January 1993.

Norton Healthcare asked that consideration be given to the wider ramifications of the issues raised by the Panel's decision. The Appeal Board was invited to consider the implications of any final ruling on the acceptability of the offer of free stock to secure purchases. Such a practice was undoubtedly widespread. A further example was that at a major chain of retail pharmacies it was common that open prescriptions were filled with originator product. This

was clearly the result of almost predatory discounting involving substantial figures on the part of the originators and could be regarded as constituting an offer of pecuniary advantage to effect the sale or supply of a medicine. Equivalent trading terms (again with very high discounts, larger than 40%) were also offered to dispensing doctors by many originator companies to encourage them to stock, prescribe and dispense originator medicines. There was clearly a distinction between trade discounting in its many forms when used to influence a pharmacist's decision on open generic prescriptions and one which attempted to induce a doctor to prescribe a more expensive medicine.

Norton pointed out that its scheme had no influence on the medical profession and the way the original prescription was written. It submitted that the Panel's position on the matter placed in jeopardy a great many of the industry's standard trade practices and the decision in this case could have ramifications beyond the remit of the Authority and could eventually restrict branded medicines to a fixed discount of 12½% and render them unable to compete for open generic prescriptions. Hospital and dispensing doctor discounts would also be viewed in a far more serious light as they really did get close to the major reason for Clause 18.1 of the Code which was to prevent inducements to prescribe. Clearly, gifts, discounts or free stock were all inducements which had a value and a purpose; however, in most cases excessive discounting would be the greater inducement.

The company referred to the Medicines (Advertising) Regulations (SI 1994 No 1932). In relation to inducements and hospitality "Nothing in this regulation shall affect measures or trade practices relating to prices, margins, or discounts which were in existence on 1 January 1993" and "No person qualified to prescribe or supply ... shall solicit or accept any gift, pecuniary advantage, benefit in kind..." Attention was also drawn to two sections of the EC Directive on the advertising of medicinal products for human use. Firstly "the provision of inducements to prescribe or supply medicinal products by the gift, offer or promise of any benefit or bonus whether in money or in kind.." and secondly "Existing measures or trade practices in Member States relating to prices, margins and discounts shall not be affected by this Article". The company submitted that if the Europharm scheme was a trade practice then it was allowed under the Code, the regulations and the EC Council Directive.

The company concluded that trade practices of the Europharm type were not excessive inducements when compared with other trade practices used throughout the pharmaceutical industry and what was offered could not be considered a gift as it was directly linked to a quantifiable discount against purchase.

APPEAL BOARD RULING

The Appeal Board noted that there had been changes to the Code in relation to trade practices and the like over recent years. It noted from the submission that there were a number of schemes relating to the supply of prescription medicines to purchasers.

The Appeal Board examined the Code and noted that the supplementary information to Clause 18.1 stated that "Measures or trade practices relating to prices, margins and discounts which were in existence in the pharmaceutical industry on 1 January 1993 are outside the scope of the Code and excluded from the provisions of this clause".

The Appeal Board considered that "prices", "margins" and "discounts" were primarily financial terms. The Appeal Board considered that monetary discounts such as 10% off the price were acceptable trade practices under the Code. Similarly 13 packs for the price of 12 was a form of discount and would be acceptable. There was a point at which these trade practices might become inducements to purchase but as long as they were reasonable such trade practices which had been used prior to 1 January 1993 would be exempt from the Code.

The Appeal Board considered that it was not acceptable under the Code to offer mountain bikes and Marks & Spencer's vouchers as a form of discounting. These were personal benefits not related in any way to the practice of medicine or pharmacy. They could not be regarded as relating to prices, margins and discounts. There was a difference between supplying vouchers for Marks & Spencer's and supplying "13 for the price of 12". The Appeal Board considered that the offer of the Marks & Spencer's vouchers and mountain bikes in the advertisement was an inducement to health professionals to purchase prescription medicines. The Appeal Board upheld the Panel's ruling that Norton Healthcare was in breach of Clause 18.1 of the Code.

The appeal therefore failed.

The Appeal Board accepted that its decision in this case would have important consequences. It did not accept that its decision would affect the acceptability of discounting in any form as submitted by Norton Healthcare. Its decision merely meant that the offer of personal goods such as vouchers for high street stores etc was not acceptable in relation to the purchase of prescription medicines. The Appeal Board requested that all the companies operating schemes referred to by Norton Healthcare in its submission were contacted by the Authority to advise them of the outcome of this case.

FURTHER CONSIDERATION BY THE APPEAL BOARD

Following the Appeal Board's decision to uphold the Panel's ruling of a breach of Clause 18.1, Norton undertook to ensure that it was no longer linked to the activities ruled in breach but made no commitment to avoid a similar breach of the Code in the future as required by Paragraph 7.1 of the Constitution and Procedure. The Appeal Board decided to report Norton to the ABPI Board of Management in accordance with Paragraph 11.1 of the Constitution and Procedure for failure to supply an adequate undertaking and for the ABPI Board to consider whether further sanctions should be applied.

REPORT TO ABPI BOARD OF MANAGEMENT

In view of the importance of the matter, the ABPI took leading counsel's opinion before the report was considered by the ABPI Board. Counsel considered that the procedures adopted by the Authority in relation to the case had been proper and was of the opinion that the Panel's ruling, endorsed by the Appeal Board, was

correct. Counsel commented that the wording of the Code in this area was somewhat opaque.

When the ABPI Board considered the matter, it noted that Norton had resigned from the ABPI because of the decision and that Norton had failed to give an adequate undertaking in the matter. Furthermore, Norton had indicated that it no longer accepted the jurisdiction of the Authority. The ABPI Board regretted the attitude which had been adopted by Norton in the matter but decided to take no further action in view of counsel's comment that the relevant requirements of the Code were somewhat opaque. As Norton had indicated that it no longer accepted the jurisdiction of the Authority, any further complaints about it would be passed on by the Authority to the Medicines Control Agency.

The ABPI Board asked the Authority to review Clause 18 of the Code to see whether its requirements could be clarified.

Proceedings commenced	**15 April 1996**
Appeal Board ruling on appeal	**23 May 1996**
Further consideration by	
Appeal Board	**10 July 1996**
Report considered by ABPI Board	**10 September 1996**

CASE AUTH/434/5/96 *NO BREACH OF THE CODE*

GENERAL PRACTITIONER v GLAXO WELLCOME

"Dear Doctor" letters on Imigran-50

A general practitioner alleged that an Imigran - 50 mailing sent by Glaxo Wellcome was disparaging of a paracetamol/codeine/buclizine combination product and another mailing made disparaging references about a paracetamol and metoclopramide combination compared to Imigran-50.

The Panel considered that the comparisons were supported by the data and were capable of substantiation. They were not misleading or disparaging and no breach of the Code was ruled.

The complaint concerned two "Dear Doctor" letters sent by Glaxo Wellcome UK. The first "Dear Doctor" letter (ref HM3101-FP/January 1996) compared Imigran-50 with an analgesic/anti-emetic combination such as paracetamol and metoclopramide. The second "Dear Doctor" letter (ref HM3135-CP/April 1996) was accompanied by a leaflet (ref HM3136 - CP/April 1996) and referred to an over the counter (OTC) combination treatment containing paracetamol, codeine and buclizine.

COMPLAINT

A general practitioner sent the "Dear Doctor" letter and the leaflet which referred to the paracetamol/codeine/buclizine combination. The complainant alleged that the mailing was disparaging. He pointed out that the letter did not mention the product by brand name but there was only one brand of this combination. The complainant alleged that this might contravene the Code. The complainant said that Glaxo Wellcome had also sent promotional material making disparaging references about a paracetamol and metoclopramide combination compared to Imigran-50, which he thought also contravened the Code.

RESPONSE

Glaxo Wellcome pointed out that only one letter was provided by the complainant but the allegations referred to two letters of similar format. The letters did not mention the competitor products by brand name.

Glaxo Wellcome said that the clinical trial programme for Imigran was the largest ever conducted for a migraine treatment. It consisted of a number of large international multi-centre controlled clinical trials with a consistent approach throughout. Including 62 corporate trials encompassing over 11,500 patients treating over 58,000 migraine attacks. In contrast trials of older migraine drugs were often uncontrolled, open labelled and too small to have adequate statistical power.

One letter stated "If these patients are taking an OTC combination treatment containing paracetamol, codeine and buclizine - as many migraineurs do - they may be continuing to suffer unnecessary migraine pain". The claim was referenced to clinical studies on the efficacy of the combination which supported the claim. Glaxo Wellcome stated that it was not disparaging to present the results of clinical studies which were unfavourable to another company's product provided they were factual, accurate and based on all the evidence. It submitted that this was so.

Paracetamol used in combination with other analgesics was a common OTC preparation used by migraineurs. Patients had expressed dissatisfaction with this analgesic. A meta analysis was used to support this claim, in which the analgesic combination of paracetamol, codeine and buclizine was rated good or excellent by only 25% of the patients (n=530). For the 307 patients treated with a combination of paracetamol and metoclopramide only 19% rated this treatment as good or excellent. 88% of patients who used sumatriptan (Imigran) as an acute medication rated it as good or excellent (n=688). The only published placebo controlled study of the combination of paracetamol and metoclopramide in the treatment of acute migraine showed no significant difference in severity of pain after treatment between the placebo group and the treated group. Further data was referred to in support of the leaflet.

RULING

It appeared to the Panel that the complainant was under the impression that it was unacceptable under the Code for a company to make adverse comments about competitor products. The Panel noted that it was acceptable for companies to make adverse comments about competitor products providing such critical references were accurate, balanced, fair and could be substantiated. This was reflected in the supplementary information to Clause 8.1 of the Code.

The Panel examined all the evidence submitted by Glaxo Wellcome to support the claims comparing the combination of paracetamol, codeine and buclizine and the combination of paracetamol and metoclopramide with Imigran. The Panel considered that the claims were supported by the data and were capable of substantiation. The Panel did not accept that the mailings were misleading or disparaging. No breach of Clauses 7.2, 7.3 and 8.1 was ruled.

Complaint received 28 May 1996

Case completed 8 July 1996

CASE AUTH/435/5/96

SCHWARZ PHARMA v BOEHRINGER INGELHEIM

Cost comparison chart in Motens detail aid

Schwarz complained about a cost comparison chart in a Motens detail issued by Boehringer Ingelheim. Schwarz said that the chart was misleading and unfair as it failed to display signifantly less expensive products. The company referred to its product Plendil which was cheaper than the products in the chart.

The Panel accepted that it was reasonable for Boehringer Ingelheim to include the costs of selected products only and for Plendil to be excluded given its small market share. Conversely, however, the chart should have included those relevant products which had a larger market share such as nicardipine and verapamil. The Panel ruled that the chart was misleading in breach of the Code as the basis of the product selection was not fair and had not been made clear.

COMPLAINT

Schwarz Pharma Limited submitted a complaint about a cost comparison chart which appeared in a Motens detail aid issued by Boehringer Ingelheim Limited. The chart compared the cost of Motens with nifedipine LA, captopril, diltiazem LA and amlodipine. Nifedipine LA 30 mg daily was the cheapest product at £10.36 and the most expensive at a dose of 90mg daily costing £25.76.

Schwarz pointed out that the cost comparison chart failed to take into account its product Plendil (felodipine) which was significantly less expensive on an equivalent daily dosage basis at £8.12 for 5mg and £10.92 for 10mg. The company said that it was important to represent the full range of less expensive alternatives as the chart might be considered to be misleading and unfair by failing to display significantly less expensive products. A breach of Clause 7.2 of the Code was alleged.

RESPONSE

Boehringer Ingelheim pointed out that the complaint concerned one page from the detail aid which was used in its entirety by representatives when detailing Motens to doctors. The company submitted that the products compared in the chart did not constitute an exhaustive list of calcium antagonists nor was there a requirement for the company to provide such a list. The list included a representative ACE inhibitor and was not therefore confined to one class of hypotensive. The company submitted that it was not misleading not to include all the other ACE inhibitors and by implication, diuretics and beta blocking agents. The chart included the market leading product as being proper to compare with Motens. Thus doctors might compare the costs of Motens against those products most commonly prescribed for the treatment of hypertension after diuretics and beta blockers. It did not regard Plendil as being appropriate for the purposes of the comparison as it was a considerably smaller product both in volume and sales. The company provided data to support this point.

Boehringer Ingelheim pointed out that the next page in the detail aid showed that Motens was compared with Plendil among other calcium antagonists. The page in question showed trough/peak ratios for Motens, felodipine, verapamil and nifedipine SR. The company submitted that in view of the importance attached to trough/peak ratios by the Food and Drugs Administration (FDA) in determining efficacy throughout the dosing interval, it was not surprising that it showed the data in a relevant setting on the relevant page. Thus it excluded felodipine as being inappropriate to the cost comparison on the previous page. The company submitted that it had neither misled nor failed to take account of the totality of the data in excluding a product shown not to have a characteristic possessed by Motens that was regarded as important by a leading regulatory agency.

RULING

The Panel noted Boehringer Ingelheim's comments with regard to the page showing trough/peak ratios. It did not consider that this was relevant to the complaint.

The Panel noted that the actual complaint was that felodipine (Plendil) had not been included in the cost comparison chart and the full range of less expensive alternatives should be included.

The Panel noted that a previous case, AUTH 412/3/96, had covered a similar matter, being the omission of

felodipine from a price comparison chart. In that case the Panel had ruled that the exclusion of felodipine was reasonable, given its very small market share.

Turning to the case now before it, the Panel noted that the chart had referred to five once daily or twice daily products at various doses. It was not stated what the prices given in the chart were for but they appeared to be for the cost of 28 days treatment for hypertension. It was not unreasonable for the costs of selected products only to be shown or for Plendil to be excluded, given its small market share. The Panel considered, however, that where a selection had been made in a comparison chart, then the basis for selection should be stated and needed to be fair. There was no information regarding the basis of selection. The Panel noted from the data provided by Boehringer Ingelheim that verapamil and nicardipine both had a larger market share than Motens but both had been omitted from the chart.

The Panel considered that as the company had omitted Plendil because it had a smaller market share than Motens, then conversely the chart should have included those relevant products which had a larger market share than Motens, ie, nicardipine and verapamil. Further, these two products were less expensive than Motens when all three were compared at their highest and lowest daily doses, eg, Motens 2mg daily, £10.66; nicardipine SR 30mg twice daily, £10.33; verapamil SR 240mg daily £10.64; Motens 6mg daily £25.16; nicardipine SR 60mg twice daily £20.66 and verapamil SR 240mg twice daily £21.28.

The Panel considered that the chart was misleading as the basis of the product selection was not fair and had not been made clear. A breach of Clause 7.2 of the Code was ruled.

Complaint received **29 May 1996**

Case completed **17 July 1996**

CASE AUTH/436/6/96 *NO BREACH OF THE CODE*

SOLVAY v E MERCK

Promotion of FemSeven

Solvay alleged that the promotional materials used by E Merck in relation to the promotion of its product FemSeven were such as to cause confusion between FemSeven and certain of Solvay's own products, such as Fematrix and Femoston. This arose principally through the "Fem" prefix itself, the use of a stylised female symbol, the use of a "charcoal" effect symbol and the use of the colour yellow.

The Panel accepted that there had been some confusion among doctors between FemSeven, Fematrix and Femoston but there was no way for knowing for certain the reasons for this or of quantifying it. Both companies had used the female symbol but Solvay's consisted of an nearly complete circle with the letter "F" at its base whereas Merck's was an octagon with a continental 7 at its base. A notable distinction was that whereas Solvay used its symbol discreetly, Merck used its symbol as the dominant feature of its materials.

Notwithstanding the commonality of certain features of the promotional campaigns, the Panel did not consider that Merck had adopted features of Solvay's promotion in a way that was likely to mislead or confuse. The promotional materials were readily distinguishable. The Panel ruled no breach of the Code.

COMPLAINT

Solvay Healthcare Ltd complained about E Merck Pharmaceuticals' promotion of its hormone replacement therapy (HRT) product, FemSeven. Solvay alleged that this was in breach of Clause 9.3 of the Code which stated that promotional material must not imitate the devices, copy, slogans or general layout adopted by other companies in a way likely to mislead or confuse.

Solvay provided a number of examples of its promotional material for Fematrix, Femoston, Duphaston and Zumenon and of Merck's promotional material for FemSeven to support the allegation. The company also provided a document headed "Evidence of Confusion" which detailed twenty-seven instances whereby doctors (both general practitioners and hospital doctors) pharmacists (both retail and hospital) a practice nurse and a medical secretary were confused between Solvay's "Fem" products and Merck's FemSeven and as to which company made FemSeven.

Solvay said that it had been active in the HRT field since 1994 with Duphaston and since that time a considerable proportion of its national and international research had been put into that field. Zumenon was launched in 1992 and the culmination of Solvay's efforts in this area was the launch of Fematrix in April 1995, Femoston in hospitals in September 1995 and to general practitioners in January 1996 and Femapak in February 1996. A considerable amount of money had been spent promoting the Solvay portfolio of HRT products in conjunction with the stylised female symbol which incorporated an upper case "F" in place of the traditional crossed vertical line. Solvay had also used the female symbol in an unstylised form in its brand names for Zumenon and Duphaston.

On 31 January 1996, some nine months after the launch of Fematrix and four months after the launch of Femoston, Merck launched its own HRT product under the name FemSeven. The promotional material used a yellow shade associated with Femoston and in some instances also included a female symbol drawn in the traditional style but in which the symbol was drawn in a "charcoal" effect.

It was well settled that the likelihood of confusion and deception arose not when two marks, products or advertisements were placed side by side and compared in detail but where a person had obtained a general impression or had merely taken in a significant detail and had retained an inaccurate record.

The promotional campaign backed by Solvay's substantial

reputation in the field of HRT resulted in its "Fem" products quickly establishing a strong position in the market. Solvay first realised that Merck had launched FemSeven in February 1996, when a series of advertisements appeared under the headline: "FEMILIARISE yourself with our new seven-day HRT patch". This advertisement used the yellow background associated with Femoston, laid emphasis on the Solvay "Fem" prefix and used a stylised female symbol which was confusingly similar to the Solvay stylised female symbol. Since that date, Merck had continued to advertise FemSeven in various medical journals and had in addition produced and distributed promotional materials bearing the confusingly similar stylised female symbol. Solvay was informed that additional promotional material existed but it had not been able to obtain samples for submission.

That Merck's actions had caused an abundance of confusion was clear from the document headed "Evidence of Confusion" which made it apparent that the combination of:

1 the use of the "Fem" prefix and in particular the play on it in the advertising;

2 the use of the confusingly similar stylised female symbol;

3 the use, in some instances, of the "charcoal" effect female symbol, and

4 the use of certain colour schemes in its advertising and promotional materials

had resulted in the "FemSeven" advertising both misleading and confusing health professionals and practitioners. In particular:

1 "Fem" prefix.

As already stated, Solvay had expended considerable resources and incurred substantial costs in developing a recognised brand name and style for its HRT range. The comments made by doctors and health professionals supported its belief that "Fem" was now firmly associated with Solvay Healthcare.

2 Stylised female symbol

Solvay had adopted a particular stylised form of the symbol to enable it to develop a recognised brand name and style for its HRT range. Once a particular symbol became associated with one company, it was human nature that if any similar symbol was used, it was unlikely to be scrutinised for distinguishing features and confusion was likely to occur. Again reference needed to be made to the comments made by doctors and health professionals. This was particularly so in the case of the symbol adopted by Merck because of the use of the continental seven, which was a mirror image of the Solvay upper case "F" used in its own symbol.

Solvay was, until the launch of Merck's product, the only company to use the female symbol in the HRT field. The female symbol was used to its knowledge in one contraceptive pill and one progestogen product.

3 "Charcoal" effect symbol

Merck used the traditional style female symbol in certain items but drawn in a "charcoal" effect. The Solvay symbol was likewise drawn in a similar faint style.

4 Colour schemes

Solvay had consistently adopted various colour schemes for its promotional material, in particular yellow for Femoston. This yellow colour, in conjunction with the "Fem" prefix and female symbol, had established a recognised Solvay brand image. The use by Merck of a similar yellow, which was already associated with Solvay, was confusing and added to the overall problem of "subliminal" association.

RESPONSE ON THE QUESTION OF JURISDICTION

Merck said that before answering Solvay's objections, it felt that it was fair to point out that this matter, in particular the use of the prefix "Fem" and the stylised version of the female symbol, had been raised with Merck by Solvay's solicitors some time ago. Merck's solicitors had answered the objections but nothing further had been heard from Solvay's solicitors. A copy of the letter from Merck's solicitors was provided. Merck felt that the Authority would understand the gravity of the case and appreciate that Solvay was asking, among other things, that the Authority prevent Merck from using the legally applied trade mark for its product. The matter of the freedom to use a particular product name was initially in the field of responsibility of the Medicines Control Agency (MCA), in dealing with applications for product licences, and subsequently a matter governed by the law of registered trade marks and passing-off. The FemSeven name had been accepted by the MCA.

On the question of whether this name constituted any infringement of Solvay's trade mark rights, Merck had answered Solvay's allegations in that respect and Solvay had not pursued that objection. The issue of whether Solvay was in a position to prevent third parties using derivations of the female symbol was likewise a matter for the law of trade marks and passing off. Indeed, this formed part of its original objection. Again, this had been answered and not pursued by Solvay. In particular, Solvay had been invited to provide details of the confusion which it alleged was occurring as a result of Merck's use of the FemSeven name and stylised female symbol - again, no response had been received to this request.

Although Solvay had now submitted to the Authority brief details of alleged instances of confusion, Merck submitted that the veracity and reliability of such evidence could only properly be tested in the legal context in which Solvay first raised the issue of confusion and not by way of complaint under the Code.

In summary, Merck suggested that this was not a case which should be answered under the Code and therefore should not proceed to a Panel decision as allowed under Clause 6.1 of the Constitution and Procedure. Should the Authority disagree, Merck would like it to consider the arguments set out in a further reply, although these of necessity reflected the position on this issue as set out above.

PRELIMINARY CONSIDERATION BY THE PANEL

The Panel noted that Clause 9.3 of the Code stated that

"Promotional material must not imitate the devices, copy, slogans or general layout adopted by other companies in a way that is likely to mislead or confuse." The Panel considered that the essence of this was the limitation at the end of the Clause which stated ".... in a way that is likely to mislead or confuse".

The Director of the Authority did not consider that this was an instance where he should rule that there was no *prima facie* case, as suggested by Merck in its reference to Paragraph 6.1 of the Constitution and Procedure. There was a *prima facie* case to answer.

The Panel considered that notwithstanding Merck's submission on the question of the approval of the product name and the use of a trade mark, it was quite proper for it to consider the allegations under Clause 9.3. Accordingly, the full submission submitted by Merck needed to be considered.

RESPONSE TO THE COMPLAINT

Merck said that Solvay argued that the test was whether a casual glance through Merck's promotional material and through Solvay's would lead to confusion between the two. Taking into account that both companies' campaigns were for similar products in the same therapeutic area, it was remarkable how different the two campaigns were. The essence of Solvay's legal complaint was necessarily also based on the premise that confusion would arise as a result of Merck's product name and advertising. In refuting this allegation, Merck requested evidence of the confusion referred to. No response had been received to that request. Had the supposed evidence of confusion provided by Solvay with its complaint to the Authority been sufficiently reliable to stand up to legal scrutiny, presumably this would have been presented to Merck to further Solvay's legal claims. The majority of pharmaceutical advertising in the HRT field had involved images of women, in particular images of young looking women leading an active life and the Solvay campaign had largely followed this trend.

Merck had been determined to be different and to produce a campaign which would stand out from other advertising in the field. Its material used two dimensional, simplistic, "road sign" type imagery and was designed to be different. Merck's material was meant to be and was eye-catching simply because it was so very different from nearly all of the advertising used for pharmaceuticals.

1 The "Fem" prefix.

Solvay contended that the "Fem" prefix belonged to it. The issue of acceptability for use of a particular product name was a matter initially dealt with upon application to the MCA for a product licence. Thereafter, this was a matter governed by the law of trade marks and passing-off. Advice given to Merck was that Solvay did not own rights in connection with the use of the "Fem" prefix such as could prevent its use by others in the context. The "Fem" prefix was not used currently solely by Solvay and there were a number of prescription products which used it, including products for HRT, analgesics, antifungals, female condoms and oral contraceptives. A list was provided. The number of non-prescription products that used the prefix "Fem" was countless.

Prefixes which had a relevance to a particular therapy or had an English meaning would be used repeatedly by different companies. A quick glance through the index of the British National Formulary demonstrated clearly that this practice was common place. Examples were too numerous to list but a few examples were given including the prefixes "Aero", "Arthro", "Calci" and "Derm".

The use of the prefix "Fem" was no more likely to confuse doctors and pharmacists than the host of other similar names, similar either by prefix or ending, that occurred among pharmaceutical products. International non-proprietory names (INN) were purposefully identical in their ending within a class in order to define a class. For example, the ending "olol" for the numerous beta blockers that were available and the ending "pril" for the more than a dozen ACE inhibitors. Doctors and pharmacists were therefore well versed in distinguishing products that had similar names. The importance of accuracy with regard to the names of pharmaceuticals was well known to both professions and was a key component in their training. This need for accuracy was well demonstrated by names beginning with the prefix "Estr".

2 Female symbol

Solvay's objection to Merck's use of a stylised version of a universal female symbol was on the basis that Merck's use of such symbols would give rise to confusion and therefore amounted to passing off.

The stylised female symbol used by Solvay was very different from that used by Merck and was not even a mirror image as it claimed. Solvay's image used a circle with an "F" protruding into the centre of the circle while Merck's consisted of an octagon with a continental seven which did not intrude into the octagon at all. Further, Solvay's symbol was not comparable in size or use with the Merck symbol. Merck's symbol acted as a border for its promotional claims, was very large and, indeed, its advertisement was the female symbol. In the Solvay advertisements, the female symbol formed part of the Solvay Healthcare logo and was a tiny image in the corner of the advertisement.

The female symbol was used in the advertising of gynaecological products not only by Merck and Solvay. The symbol and its derivations were widely used.

Such repeated use of a relevant image within a therapeutic area was almost inevitable where such a strong image existed. Another example was cardiovascular medicine, where the image of the heart was used repeatedly as part of the main imagery or as a logo.

3 The "charcoal" effect as applied to the symbol.

Solvay used a stylised female symbol with a thick hazy outline which it referred to as a "charcoal" effect, specifically for all its HRT products. Merck used a broken outline for its own symbol (of a quite different appearance) and only where the symbol was used to denote osteoporosis (the lace like appearance of oesteoporotic bones). This appeared only in a minority of Merck's promotional material. In the same way, in some of Merck's other materials, a derivation of the female symbol in the form of a heart was used to denote cardiovascular indications. Again, this "osteoporosis" female symbol was dissimilar to the logo used by Solvay

in terms of size, its use as part of the main image and its detailed composition.

4 The colour yellow.

In the same way in which Solvay appeared to be claiming (without justification) to have a right to prevent others from having use of product names with a "Fem" prefix, it seemed to be making a similar claim to a monopoly to use the colour yellow. There was no basis for any such right. In particular, Solvay had not even established a universal yellow image for its advertising of gynaecological products (or even across its range of HRT products).

The colour used in Merck's advertising campaign was not based on a yellow colour scheme throughout. Rather the colours of the campaign were bright yellow, deep red, bright blue and deep purple. Its promotional campaign was associated with bright colours rather than with any particular colour.

Up to the end of May, Merck had used the "Femiliarise" advertisement which was yellow twenty times, the "looking for" advertisement which was red nine times, the "sad/happy" advertisement which was blue six times, the "stick around" advertisement which was yellow nine times and the "cardiovascular" advertisement which was red and yellow thirteen times. The "osteoporosis" advertisement which was purple was due to be introduced in June and would account for twenty-two of the planned fifty-eight appearances with the "cardiovascular" advertisement - yellow and red - taking up a further twenty-three.

None of Merck's market research had suggested that the FemSeven campaign was in any way confusing or misleading with respect to Solvay (the company or any of its brands). This research focused on the product name and the use of the stylised female symbol and also the advertising imagery. Its independent research included data from five studies involving a total of one to two gynaecologists and two to five general practitioners. One of the criteria used in choosing a name for its product was a low score for confusion with other products as measured by market research. A summary of the data was supplied.

RULING

The Panel observed that the MCA had permitted FemSeven to be used as the name of Merck's product. It was not for the Panel to express any opinion as to the appropriateness or not of the product name or to concern itself with trade mark rights and "passing-off" or any other similar matters. The same considerations applied to the question of what legal rights, if any, Solvay had with respect to the female symbol and the colour yellow in the manner in which they had been used. The sole matter for the Panel to consider was whether, in its opinion, any or all of these had been used by Merck in a way that was likely to mislead or confuse.

The Panel examined all of the promotional materials which had been submitted by Solvay and Merck and noted that there were some features in common. The "Evidence of Confusion" document submitted by Solvay showed that some doctors were confused as between FemSeven, Femoston and Fematrix. In some of the reported instances, however, it seemed that it was the commonality of the prefix "Fem" which had given rise to the confusion and that was not a matter which was within the province of the Panel. The Panel acknowledged that there had been some confusion but there was no way of knowing for certain the reasons for it or of quantifying it.

Both companies had used a female symbol, that used by Solvay consisting of a nearly complete circle with a letter "F" at its base. Merck's symbol used an octagon rather than a circle with a continental 7 at its base. A notable distinction between the two companies' promotional materials was that whereas Solvay used its symbol discreetly, usually in a small size at the bottom of the page, Merck used its symbol as the dominating feature of its materials with the copy often appearing within the octagon. Both companies had sometimes used a variant of the female symbol in the roughened style they referred to as the "charcoal" effect but in Merck's case only in relation to osteoporosis where the company had used a standard symbol in the "charcoal" effect rather than its usual octagon.

Notwithstanding the commonality of certain features of the promotional campaigns, the Panel did not consider that Merck had adopted features of Solvay's promotion in a way that was likely to mislead or confuse. The promotional materials were readily distinguishable. It was accordingly ruled that there was no breach of Clause 9.3 of the Code.

Complaint received **3 June 1996**

Case completed **29 July 1996**

HOSPITAL PHARMACIST v SMITHKLINE BEECHAM

Unsolicited supply of Famvir

A hospital pharmacist complained about the unsolicited supply of a Famvir pack by SmithKline Beecham.

The Panel ruled no breach of the Code as the pack had been sent in 1995 before the Code was amended to require that unsolicited medicines must not be sent through the post.

COMPLAINT

A hospital pharmacist complained about a letter received from SmithKline Beecham Pharmaceuticals UK. The letter referred to Famvir being available for genital herpes and a complimentary treatment pack for use by the hospital's centre for sexual health was included.

The complainant alleged a breach of Clause 17.10 of the Code as the pack had been sent unsolicited through the post.

RESPONSE

SmithKline Beecham said that it had not supplied any complimentary treatment packs in this manner since May 1995. On checking its records, it appeared that the letter in question dated back to April 1995 when Famvir was launched for the treatment of genital herpes. The company could not explain why the complaint had been made a year after the mailing.

RULING

The Panel noted that there had been a complaint in 1995 about the letter in question. It had been decided that the supply of the pack was the supply of free goods as part of commercial trading practice and did not constitute a gift or inducement prohibited under the Code and no breach had been ruled.

The Panel noted that the requirements regarding the sending of unsolicited medicines through the post had changed. The 1994 edition of the Code prohibited companies from sending unsolicited starter packs through the post. The 1996 Code had expanded this prohibition and Clause 17.10 required that unsolicited medicines must not be sent through the post.

The Panel noted the submission that the letters had not been sent since May 1996. The 1996 requirements of the Code did not apply retrospectively to an activity in May 1995. The Panel therefore ruled no breach of the Code.

Complaint received **5 June 1996**

Case completed **18 July 1996**

CASE AUTH/439/6/96

DIRECTOR v JANSSEN-CILAG

Breach of undertaking

Two instances involving breaches of an undertaking given by Janssen-Cilag in relation to the promotion of Topamax were drawn to the attention of the Code of Practice Authority. The items concerned were a journal advertisement (Case AUTH/378/11/95) and a number of slides containing a table (Cases AUTH/378/11/95 and AUTH/391/1/96).

The Panel ruled no breach of the Code regarding the alleged use of slides by Janssen-Cilag representatives as there was no evidence that the representatives had continued to use the slides after being instructed to cease their use.

The Panel considered that the use of the journal advertisement in Hospital Doctor, just less than a month after the date of the company's undertaking to discontinue the advertisement forthwith, meant that the company had failed to comply with an undertaking. A breach of the Code was ruled. The Panel also ruled that the company's tardiness in complying with its undertaking brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

Janssen-Cilag appealed the ruling of Clause 2 on the basis that the failure to comply was due to human error. The Appeal Board agreed with the Panel and upheld its ruling of a breach of Clause 2.

COMPLAINT

Parke Davis & Co Limited complained that Janssen-Cilag was continuing to use an advertisement for Topamax (topiramate) which had previously been ruled to be misleading in breach of Clause 7.2 of the Code (Case AUTH/378/11/95). Parke Davis said that some Janssen-Cilag representatives were using a number of slides containing a table which had been ruled to be misleading in breach of Clause 7.2 of the Code in that the impression given was that the data was from directly comparative studies and this was not so (Cases AUTH/378/11/95 and AUTH/391/1/96). Parke Davis stated that it understood that Janssen-Cilag representatives had been told that they could supply the table to doctors as long as it was not used to sell topiramate.

In view of the fact that the complaint involved possible breaches of undertaking, the matter was taken up as a complaint by the Director of the Authority as the Authority itself was responsible for ensuring compliance with undertakings. This accorded with guidance previously given by the Appeal Board.

RESPONSE

Janssen-Cilag said that due to an oversight the advertisement found to be in breach of the Code appeared in Hospital Doctor, 25 April 1996. Following the undertaking given by the company (dated 27 March 1996) that it would withdraw the advertisement, the appropriate journals were informed and an amended advertisement was placed. Regrettably there was a delay in implementing this change with Hospital Doctor and the company accepted that it was in breach of Clause 21 in not ensuring prompt compliance with the undertaking.

The company provided a schedule of events. The advertising copy changes were approved by Janssen-Cilag on 26 March 1996, the art work was provided by the agency on 4 April, revised art work was provided on 11 April, proofs were provided on 17 April and the revised films were supplied to the publishers on 25 April. The lead time for Hospital Doctor, a weekly publication, was ten days. The revised advertisement for Topamax appeared in Hospital Doctor on 2 May and in the June editions of the British Journal of Psychiatry and the Journal of Neurosurgery and Psychiatry.

The company took action to replace immediately the Topamax advertisement ruled in breach. However, it might have been more prudent given the long lead times for the journals to remove it totally showing blank space.

With regard to the second allegation about the continued use by representatives of slides containing the table ruled to be misleading, the company stated that its representatives were at a training meeting for a week commencing 25 March. They were notified on their return to normal working on 1 April to stop using any material containing the comparison table. The representatives had been advised by e-mail on 31 March 1996 and instructed to destroy all remaining monographs in their possession, to cease use of the comparative table in the sales aid and to cease use of the comparative table in the set of presentation acetates. A copy of the e-mail was provided by the company.

PANEL RULING

The Panel examined the undertaking given in Cases AUTH/378/7/95 and AUTH/391/1/96. It had been signed and dated 26 March 1996 by the Managing Director. One of the sections of the form of undertaking referred to the requirement for discontinuation of the material or withdrawal from use forthwith. This had been completed by another person. The last date on which the material was used was given as 27 March 1996 and this other person had corrected the date given in relation to the Managing Director's signature from 26 March to 27 March. It appeared to the Panel that the company had not paid sufficient attention to the undertaking and what was required. It had been completed without a proper

appraisal of the situation as regards journal advertisements.

The Panel noted that the company's representatives had been instructed by e-mail on 31 March to cease using the comparative table in their sets of acetates. At the time the undertaking was signed the representatives were at a training meeting all week and would have received the e-mail before returning to the field on the Monday following the training course (1 April 1996). There was no evidence that representatives had continued to use the acetates or that they had been told that they could supply the table to doctors as long as it wasn't used to sell Topamax, as stated by Parke Davis. The Panel therefore ruled no breach of the Code in that regard.

With regard to the advertisement in the 25 April issue of Hospital Doctor, the Panel noted that the publication had a ten day lead time. It considered that Janssen-Cilag had had sufficient time to provide the new advertisement to Hospital Doctor for the 25 April issue given that the copy would have to be at the publishers by 15 April which was more than two weeks after the date of the undertaking (27 March). If the deadline could not have been met with a new Topamax advertisement, the company could have arranged for another advertisement to be used in the booked space. The Panel considered that the slowness of the company in withdrawing the advertisement meant that the company had failed to comply with its undertaking. The Panel therefore ruled a breach of Clause 21 of the Code as acknowledged by the company.

Failure to comply with an undertaking was a serious matter. In the Panel's view the company had attempted to comply with the undertaking but it had been too slow. In the Panel's view the failure to comply with the undertaking was not due to human error as in a previous case (AUTH/185/7/94) in which the Appeal Board had overturned the Panel's ruling of a breach of Clause 2 of the Code. In the case now before it the Panel decided that the company's tardiness in complying with its undertaking brought discredit upon and reduced confidence in the industry and therefore a breach of Clause 2 of the Code was ruled.

The Panel noted that the Constitution and Procedure required it to report a company to the Appeal Board if it failed to comply with the procedures or if its conduct in relation to the Code warranted consideration by the Appeal Board (Paragraphs 8.1 and 8.2). The Panel decided that the circumstances did not warrant reporting Janssen-Cilag to the Appeal Board.

APPEAL BY JANSSEN-CILAG

Janssen-Cilag accepted that it was in breach of Clause 21 of the Code but appealed the Panel's ruling of a breach of Clause 2 of the Code.

Janssen-Cilag submitted that Clause 2 was reserved as a sign of particular censure and was infrequently ruled. The Panel had decided that the company's tardiness in complying with the undertaking brought discredit upon and reduced confidence in the industry. Janssen-Cilag disputed this. The company submitted that the breach of undertaking was due to human error by one individual who had been severely reprimanded and, whilst fully accepting its responsibilities for the individual's actions in the circumstances, a Clause 2 censure was inappropriate.

The company had reviewed recent cases where a Clause 2 breach had been ruled. It drew particular attention to Case AUTH/185/7/95 where the Panel had ruled a breach of Clause 2 for failing to comply with an earlier undertaking but this had been overturned upon appeal with the Appeal Board noting that the breach of undertaking had arisen as a result of human error. The company also drew attention to Case AUTH/31/4/93 in which the Panel had noted that the company had taken steps to implement its undertaking, and accepted that the use of the material had been an error. The Panel had ruled in this instance that there had been no breach of Clause 2 of the Code.

Given the established precedents for the use of Clause 2, Janssen-Cilag submitted that the error on behalf of one of its staff was not in the same category as falsifying expense accounts, distributing pornographic videos etc. Additionally the precedents of Cases AUTH/185/7/94 and AUTH/31/4/93 would argue that a single error by a member of staff, with there being evidence of the company otherwise adhering to the undertaking, would suggest that a Clause 2 censure in this case would be inappropriate.

Janssen-Cilag was slightly mystified about the Panel's comments that the failure to comply was not due to human error. The advertisement in question had appeared in the British Medical Journal and in Hospital Doctor. Following its undertaking the product manager responsible successfully ensured that the advertisement in breach did not appear in the British Medical Journal but failed to have it withdrawn from Hospital Doctor. To suggest that this was not the result of human error on the part of a single individual implied there was a wider company conspiracy to continue to place the offending advertisement. If this had been so why would the conspiracy not have included publication of the advertisement in the British Medical Journal? The company strongly refuted any suggestion of a wider company conspiracy.

The company explained the action taken by the company in that there had been a communication sent to the sales force advising that materials were to be withdrawn from use. A new advertisement replaced the old advertisement in the British Medical Journal. The error was that the new advertisement arrived too late for Hospital Doctor to replace the old advertisement and therefore the old advertisement continued. The error was in failing to cancel the old advertisement specifically. The company had immediately withdrawn the advertisement and unreservedly apologised once the error was apparent. The individual was subject to an internal disciplinary procedure and mechanisms were put in place in the company to ensure no repeat.

APPEAL BOARD RULING

The Appeal Board considered that an undertaking was an important document. It required companies to provide details of the action taken and the date of final use of materials ruled in breach. The form of undertaking was to be signed by the chief executive or

with his or her authority. It included a section in which an assurance was given that all possible steps would be taken to avoid similar breaches of the Code in the future. It was very important for the reputation of the industry that companies complied promptly with undertakings given in relation to rulings under the Code. Companies should have procedures in place to make sure that undertakings were promptly complied with. In the Appeal Board's view, companies would be well advised to issue detailed written instructions to relevant staff about the action required to ensure compliance with undertakings.

Turning to the case now before it, the Appeal Board was concerned about the arrangements within Janssen-Cilag for complying with its undertaking. It did not accept that the company had shown that the appearance of the advertisement in Hospital Doctor had been due merely to human error. The Appeal Board considered that the reuse of the advertisement was due to inadequate procedures within the company. The Appeal Board agreed with the Panel that the tardiness of the company in complying with its undertaking brought discredit upon and reduced confidence in the industry and therefore the Panel's ruling of a breach of Clause 2 of the Code was upheld.

The appeal therefore failed.

Complaint proceedings commenced **14 June 1996**

Case completed **4 October 1996**

CASE AUTH/440/6/96 *NO BREACH OF THE CODE*

LEO v E Merck

Curatoderm advertisement

Leo complained about a Curatoderm advertisement issued by E Merck alleging that "Cost saving" within the statement "Cost saving. Daily treatment costs for once daily Curatoderm compare favourably to twice daily calcipotriol" was a pharmacoeconomic claim which could not be substantiated.

The Panel did not consider that the claim was a pharmacoeconomic comparison between the two products as alleged. On a daily basis, given their licensed doses and costs, Curatoderm was less expensive than calcipotriol ointment. The Panel thus considered the claim was reasonable and ruled no breach of the Code. This view was upheld on appeal with the Appeal Board considering that the second part of the claim clearly and sufficiently indicated that the term "Cost saving" related only to daily treatment costs.

COMPLAINT

Leo Pharmaceuticals alleged that an advertisement for Curatoderm, issued by E Merck Pharmaceuticals, which had appeared in the British Journal of Dermatology, May and June 1996, was in breach of Clause 7.2 of the Code. Attention was drawn to the claim "Cost saving. Daily treatment costs for once daily Curatoderm compare favourably to twice daily calcipotriol".

Leo said that whilst price comparisons were acceptable within the Code, the claim in question was a pharmacoeconomic comparison between Curatoderm (tacalcitol) and its product, Dovonex (calcipotriol).

Within the same advertisement, claims were made in respect of the efficacy of tacalcitol. The "Cost saving" claim should take relative efficacy of tacalcitol and Dovonex into account and had failed to do so. Dovonex was in fact more effective than tacalcitol in the treatment of psoriasis and, therefore, a "Cost saving" claim could not be substantiated.

RESPONSE

Merck said that both Curatoderm and Dovonex were vitamin D analogues used in the treatment of psoriasis. Ointments had been demonstrated to cover a certain area of skin surface per gram. Curatoderm was applied once daily and Dovonex was applied twice daily according to their respective summaries of product characteristics (SPCs). While the daily treatment cost per patient could not be stated, as this would depend on the area of psoriasis to be treated, it was clear that the amount of Curatoderm required to treat any given area of psoriasis would be half the amount of Dovonex ointment required to treat the same area when applied in accordance with the dosage recommendation specified in the relevant product licences. Reference to usage, which was not approved by the UK Regulatory Authority, was of no relevance to these considerations. Such references, as already made by Leo, did of course actually breach the Code.

On this basis and according to the supplementary information given in Clause 7.2 of the Code, a fair comparison of daily treatment cost could be made by comparing the cost of one gram of Curatoderm with two grams of Dovonex.

The price of a 30g tube of Curatoderm was £15.09 compared to the 60g tube of Dovonex which was £16.30. The price of a 60g tube of Curatoderm was £26.00 compared with £29.04 for a 120g tube of Dovonex. This worked out at a cost saving of more than 7% on the smaller tubes and of over 10% on the larger tubes. The price of Curatoderm therefore compared favourably with the price of Dovonex.

Comments from Leo regarding comparative efficacy would suggest that a cost comparison could only be made where the results of a health economic study were available. This was not required according to the Code. Any claim by Leo regarding differences in efficacy or severity of disease treated was not reflected in the relevant SPCs and would therefore also be a breach of the Code.

PANEL RULING

The Panel did not accept that the claim was a pharmacoeconomic comparison between the products as alleged. The claim merely compared the costs of treatment with "once daily Curatoderm" and "twice daily calcipotriol", which were the licensed dosages for each product. The claim made no reference to individual efficacy or relative efficacy of either product. While it was not possible to quantify how much of each product a patient would use, given the licensed doses each patient applying calcipotriol ointment twice daily to an area of psoriasis was likely to use twice as much ointment than if they applied Curatoderm ointment only once daily to the same area. The cost of a 30g of Curatoderm ointment at £15.09, compared favourably to the cost of 60g calcipotriol at £16.30.

The Panel considered that the claim was reasonable and ruled no breach of Clause 7.2 of the Code.

APPEAL BY LEO

Leo believed that the claim "Cost saving. Daily treatment costs for once daily Curatoderm compare favourably to twice daily calcipotriol" was a comparative pharmacoeconomic claim in view of the claim "Cost saving". A conclusion of "Cost saving" could not be based only on a comparison of theoretical daily treatment costs.

For the claim "Cost saving" to be substantiated, it must be shown, as stated in supplementary information to Clause 7.2, that "usage rates are similar or, where this is not possible, for the comparison to be qualified in such a way as to indicate that usage rates may vary". Usage rates were dependent upon efficacy. In the absence of relative efficacy data, no assumption could be made in respect of relative usage rates. It therefore followed that the claim "Cost saving" could not be substantiated.

The advertisement was not simply a relative daily cost comparison. Neither could the cost saving claim be justified on the basis of the licensed recommended frequency of administration. The actual relative dose used for these products was not known and the cost saving claim was not substantiated.

Leo drew attention to part of the supplementary information under Clause 7.2 of the Code which stated: "To be acceptable as the basis of promotional claims, the assumptions made in an economic evaluation must be clinically appropriate .....". The claim "Cost saving" implied a financial saving. A financial saving was only possible if a given outcome was achieved. Failure to achieve a desired outcome would result in increased costs.

RESPONSE BY MERCK

Merck submitted that the basis of the appeal by Leo was that the phrase "Cost saving" made more than a cost claim and implied a health economic evaluation. To interpret such a simple phrase in this way required considerable imagination. Unlike terms such as "cost effective", "cost benefit" and "cost utility" which had come to refer to certain types of economic analysis, the term "Cost saving" had no such connotation.

Merck said that its price comparison took into account usage rates which were determined by the surface area to be treated and frequency of application. The statement made it quite clear that Merck was making a comparison of daily treatment costs.

Merck submitted that there was no hint nor suggestion in its claim that it was referring to efficacy, tolerability, convenience, quality of life or any other related parameter which could have lead to misinterpretation that it referred to a health economic analysis.

Merck submitted that health professionals were more than able to make their own evaluation of products, weighing up the benefits of cost against efficacy, tolerability etc. without the balance of these being evaluated for them.

FURTHER COMMENTS FROM LEO

There were no further comments from Leo.

APPEAL BOARD RULING

The Appeal Board noted that the claim in question was presented in two parts. There was a strap line "Cost saving" followed by qualifying text which stated "Daily treatment costs for once daily Curatoderm compare favourably to twice daily calcipotriol". Although printed in different colours, both parts of the claim were presented in a large type face. In isolation the strap line "Cost saving" would be taken to refer to total treatment costs and mean that one product had a cost advantage over the competitor. If such a claim were being made factors such as comparative efficacy, length of treatment and tolerability etc would be relevant in assessing the total treatment cost. The Appeal Board considered, however, that the text immediately beneath the strap line clearly and sufficiently limited its meaning to daily treatment costs. The Appeal Board noted that, according to the licensed doses for each product, on a daily basis Curatoderm was less expensive then Dovonex. The Appeal Board thus considered that the overall claim was acceptable and was not misleading. The Appeal Board therefore upheld the Panel's ruling of no breach of Clause 7.2 of the Code.

The appeal in this case failed.

Complaint received **19 June 1996**

Case completed **12 September 1996**

CASE AUTH/441/6/96

SETON v HOUGHS

Triclosan information document

Seton Healthcare complained that a practical information document on Triclosan and MRSA, issued by Houghs Healthcare, lacked prescribing information, promoted off licence indications and formulations and lacked supporting references.

The Panel noted that the document was part of a standard information pack supplied in response to all general enquiries. The pack contained promotional items and the information given in the document was not tailored to the needs of specific enquirers. The document was viewed as promotional and the Panel ruled breaches of the Code with respect to the lack of prescribing information and the mention of off licence indications and formulations. No breach of the Code was ruled regarding substantiation of certain claims.

Seton Healthcare Group plc complained about a double-sided A4 document issued by Houghs Healthcare Ltd, headed "Triclosan and M.R.S.A" (MRSA = methicillin resistant *Staphylococcus aureus*). The document contained a number of bullet points relating to the use of triclosan based skin antiseptics against MRSA. A number of products (Aquasept, Ster-Zac Powder, and Triclosept Cream) were mentioned. One section of the document was entitled "M.R.S.A and Neonates".

COMPLAINT

Seton Healthcare pointed out that the document, (believed to be a mailing), lacked prescribing information, promoted off licence indications eg the use of a 60% solution of Aquasept on wounds infected with MRSA and use in neonates, promoted unlicensed formulations for named patient supply and lacked supporting references. Breaches of Clauses 4.1, 3.1, 3.2 and 7.3 of the Code were alleged.

RESPONSE

Houghs Healthcare pointed out that the document was not an indiscriminate mailshot. It was one page out of a standard information pack which was only ever sent to named healthcare professionals eg infection control nurses or information pharmacists who asked for more information on Houghs' products in general or their use in MRSA in particular.

A complete information pack was provided and this consisted of several items in addition to the document in question. There was an A4 brochure entitled "Houghs Healthcare" which gave background information on the company and its products. Tucked into a pocket in the back of the brochure were several fact sheets on various products most of which included prescribing information although one detailing triclosan as an active ingredient did not. The document in question was with these fact sheets. A promotional brochure on Aquasept promoting its use in the eradication of MRSA, a small patient instruction card on the use of Aquasept and the product data sheet were also in the information pack. The Aquasept brochure had a leaflet on triclosan tucked into a flap on the back page. A data sheet for Ster-Zac Powder was also provided along with three clinical papers which looked at the control of MRSA. Finally an A4 double-sided sheet was sent, entitled "Information for Patients and Carers MRSA".

With regard to Seton's specific complaints Houghs submitted:

·Clause 4.1 - Prescribing information for each licensed product discussed in the information pack was included.

·Clause 3.1 - Off licence formulations. Houghs offered this service on the specific request of a doctor, for his/her named patient. These were not complete reformulations, but generally involved the omission of one or more excipients to which the patient had a known allergy; eg fragrance.

These samples were issued free of charge for individual patient treatment only. Houghs did not make any medical claims for these products; they were supplied at the discretion and on the clinical experience of the doctor concerned. They were supplied in a plain bottle with a computer printed label, and were accompanied by the relevant Health & Safety data sheets. Records were kept of formulation details, names, dates etc. Such requests were rare and, in fact, there had been none in recent years.

·Clause 3.2 - Off licence indications - this indication had now been removed from all its literature. This indication had been investigated by the previous qualified person, and had now been withdrawn.

·Clause 7.3 - Lack of substantiation. All claims made for Houghs' products could be and had been substantiated on the relevant product literature which was included in the complete information pack as supplied.

Houghs said that it worked very closely with the manufacturers of triclosan in substantiating all claims made.

RULING

The Panel noted that the complaint was only about the double-sided A4 document entitled "Triclosan and M.R.S.A" included in the standard information pack. The Panel noted that this document was sent out with promotional material. The document was on plain white paper and was printed in blue and red. It contained no illustrations or pack shots, only a series of bullet points. The Panel considered that the document had been produced in an attempt to provide customers with some helpful, practical information regarding the use of triclosan based products in the control of MRSA. In the Panel's view however it had gone too far. The document was supplied, with promotional items, in response to general enquiries. The pack was not tailored to the requirements of individual enquirers and so was not exempt from the Code as set out in Clause 1.2 of the Code. The document was viewed as promotional. It mentioned

Aquasept, Ster-Zac Powder and Triclosept Cream by name and prescribing information for all three products should have been included but was not. The Panel accordingly ruled a breach of Clause 4.1 of the Code.

The Panel noted that the copy of the document supplied by Seton contained a statement referring to the use of a 60% solution of Aquasept in wounds infected by MRSA. This statement was not included in the document supplied by Houghs. Both documents referred to the use of diluted Aquasept for the eradication of MRSA in neonates or full term babies. Such recommendations for use were not in the Aquasept data sheet and so the Panel ruled a breach of Clause 3.2 of the Code.

The final statement on the document "If you have problems as regards patients with skin problems or allergies, Houghs will endeavour to help by making up individual formulations for named patients" was viewed by the Panel as promoting unlicensed products. It would be different if Houghs' business was to make specials of any sort of medicine but this offer was too specific. Houghs were only offering to make special formulations of its own products. A breach of Clause 3.1 was ruled.

With regard to the eradication of MRSA, the Panel noted that the data sheets for Ster-Zac Powder and Aquasept were both silent on the point and the indications listed were relatively vague. The Panel considered that the data sheets could have been more helpful with regard to the precise indications. The Panel noted that the data sheet for Aquasept in the ABPI Data Sheet Compendium (1995-96) stated that the use of the product was as a pre-operative surgical hand disinfectant, an antiseptic skin cleanser and for the prevention of cross infection. The data sheet for Ster-Zac Powder, from the same compendium stated that the product was for the prevention of neo-natal staphylococcal cross infection, as an adjunct in the treatment of recurrent furunculosis and for routine use in midwifery. The Panel did not accept that the reference to MSRA constituted promotion of an unlicensed indication and therefore ruled no breach of Clause 3.2 of the Code. Three clinical papers were provided, which gave some evidence of the effectiveness of triclosan against MRSA. The Panel considered that the company had provided substantiation for claims relating to use in MRSA. No breach of Clause 7.3 of the Code was ruled.

Complaint received **24 June 1996**

Case completed **20 August 1996**

Case AUTH/442/7/96

JANSSEN-CILAG v PARKE DAVIS

Journal advertisement relating to previous Code of Practice ruling

Janssen-Cilag complained about an advertisement headed "Caveat Emptor" issued by Parke Davis. The advertisement referred to published Code of Practice cases involving Janssen-Cilag. Janssen-Cilag alleged that the advertisement disparaged its activities, did not recognise the high standards required for the promotion of medicines and brought discredit upon the industry. It was also alleged that no prescribing information had been given for the Parke Davis product referred to in the advertisement and that there had been a failure to properly certify the advertisement.

The Panel considered that it was not a breach of the Code to refer to previous rulings under the Code, although the manner in which it was done could breach the Code. The Panel ruled that the use of the words "Caveat Emptor" disparaged Janssen-Cilag. The use of that term and the use of an inaccurate quotation from the published case report meant that high standards had not been maintained and the Panel ruled accordingly. The absence of prescribing information for the Parke Davis product referred to in the advertisement was also ruled in breach. The Panel did not consider that there had been a failure to adequately certify and did not consider that the advertisement had brought discredit upon the industry.

Upon appeal from Janssen-Cilag, the Appeal Board ruled that the advertisement had brought discredit upon the industry. An appeal by Parke Davis in relation to the rulings that Janssen-Cilag had been disparaged, that high standards had not been maintained and that prescribing information had been omitted, was rejected by the Appeal Board which upheld the Panel's rulings.

Janssen-Cilag Ltd complained about a journal advertisement issued by Parke Davis & Co Limited. The advertisement was headed "Caveat Emptor" and had appeared in A3 size in Hospital Doctor, 27 June 1996, and in A4 size in the British Medical Journal, 29 June 1996. Each bore the reference Y120/June 1996/UK.

The advertisement bore an illustration of a wedge of cheese and sticks of chalk. The secondary heading was "Meaningful interpretation of clinical trials requires comparison of like with like" (the words "like" and "like" were emphasised by use of a larger and bolder typeface). The text beneath said that this was particularly relevant when the nature of the condition was such that a comparison between different patient groups could not be made, such as in refractory partial epilepsy, and went on to say that at present no direct comparative data existed between lamotrigine (Glaxo Wellcome's product, Lamictal), gabapentin (Parke Davis' product, Neurontin) and topiramate (Janssen-Cilag's product, Topamax).

The advertisement then stated "Despite this, a misleading comparison was made in the topiramate monograph. Recently the Prescription Medicines Code of Practice Authority (PMCPA) ruled against Janssen-Cilag on this point; `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 comparable studies and this was not so' ". This latter point was a quotation from the summary in the published report of a ruling of the Appeal Board in previous cases (AUTH/378/11/95 and AUTH/391/1/96 - Parke Davis

and hospital doctor v Janssen-Cilag), the underlining of the word "misleading" having been added by Parke Davis.

At the bottom of the advertisement, beneath the name Parke Davis, was the statement "Over 50 years experience in the management of epilepsy".

COMPLAINT

Janssen-Cilag alleged that the advertisement, as evidenced by the comments in Pharmaceutical Marketing, was in breach of Clause 2 of the Code as it brought discredit upon the industry. Janssen-Cilag alleged that the advertisement did not recognise the high standard required for the promotion of medicines and therefore breached Clause 9.1 of the Code. The advertisement also disparaged the (past) activity of Janssen-Cilag in breach of Clause 8.1.

Janssen-Cilag presumed that the advertisement was promotional for Neurontin in that the company name, Parke Davis, a therapeutic claim "Over 50 years experience in the management of epilepsy" and the generic name for Neurontin (gabapentin) were all present. No prescribing information for Neurontin had been given and therefore the advertisement was in breach of Clause 4.1.

Janssen-Cilag said that the advertisement appeared in two different sizes, one being A3 and one A4. The guidelines on company procedures (page 37 of the 1996 Code) required that each different size of promotional material should have its own unique reference number. This meant that each size of the advertisement was in breach of Clause 14 in that there could not be a unique certificate certifying compliance with Clause 14 for each size of the advertisement.

The "News line" article in the July issue of Pharmaceutical Marketing led Janssen-Cilag to believe that a mailing was being sent by Parke Davis to doctors which would presumably repeat the imagery and wording of the journal advertisements. If this was the case, then Janssen-Cilag suspected that this mailing might also breach Clauses 2, 8.1 and 9.1. This letter was subsequently the subject of Case AUTH/444/8/96.

RESPONSE

Parke Davis said that it considered the allegation of a breach of Clause 2 of the Code seriously ill-judged. The advertisement could not be considered to bring discredit on the industry. The issue was really a straightforward question on which Parke Davis would welcome debate and resolution. Should rulings under the Code be kept secret or were they in the public domain? If they were in the public domain, was there a regulation which prevented interested parties receiving the information? If not, then all the advertisement did was repeat fair copy that could equally well have appeared in the editorial of the British Medical Journal. Presumably a complaint against such an editorial could not be entertained. This clear issue of principle was in danger of being lost. Parke Davis could not be responsible for bringing the industry into disrepute by reporting non-disputable facts.

It would be difficult to understand how it might credit an industry to discourage customers from hearing the facts on companies which had been found guilty of misinforming them. Indeed, it could be argued that greater publicity enhanced the standing and reputation of the Authority. Any decision to limit such publicity would reflect very badly on an industry already regarded with suspicion. Vigorous public competition did not bring the industry into disrepute; it demonstrated the independence of the companies and accurate reporting of the truth could not be legitimately criticised. If Parke Davis was found guilty of that, then observers of the industry would indeed have grounds to charge all of the industry.

Parke Davis had taken such strong action because it was very disturbed by what it regarded as the blatant and ethically unsound action of Janssen-Cilag in this promotion and considered that it was appropriate for Parke Davis, with its long history in this therapeutic area, to redress the balance. Firstly, Parke Davis pointed out that Janssen-Cilag had failed to carry out undertakings agreed with Parke Davis in writing following its first complaint over one year ago. Janssen-Cilag had agreed to write to physicians about the misleading nature of its publication "Clinical Courier"; instead it repeated the offending misrepresentations in its product monograph. Secondly, Parke Davis maintained that Janssen-Cilag's chief executive was disinclined to discuss Parke Davis' complaint regarding the product monograph and other items before it was submitted to the Authority. Every effort was made to delay responses in order to keep questionable material in use. Thirdly, Parke Davis argued that Janssen-Cilag exploited every opportunity available to it through the Code of Practice system and, far from "respecting the spirit of the Code", it used the system to continue to promote for commercial gain while matters were being appealed. It failed to give due consideration to the needs of health care professionals and patients. (Cases AUTH/378/11/95, AUTH/391/1/96 and AUTH/389/1/96). Finally it continued to publish an advertisement after losing an appeal and signing an undertaking to cease immediately its use (Case AUTH/439/6/96).

Parke Davis' corrective advertisement did nothing to unfairly sully the name of Janssen-Cilag. Parke Davis simply delivered information of importance to clinical practice rather than leave physicians with misleading material. This was not in breach of the letter or spirit of the Code. It was an ethical action in recognition of Parke Davis' primary responsibility to patients and health care professionals.

Far from being in breach of Clause 9.1 the advertisement communicated accurate information where healthcare professionals had previously been misled so that clinical decisions in a complex therapeutic area need not be unduly influenced by flawed promotional material. The advertisements were not tasteless or unsuitable in nature.

Clause 8.1 referred to the use of disparaging references to the medicines, products or activities of other pharmaceutical companies. The statements Parke Davis had used were accurate, balanced, fair and fully justified. It had, in fact, quoted in full and accurately from the Authority's ruling.

In considering Clause 4.1, the presumption that the advertisement was promotional for Neurontin was

incorrect. This was corrective advertising in which Parke Davis' heritage was also important. The name gabapentin was mentioned, but so were those of lamotrigine and topiramate. These names were all necessary inclusions in describing the claims being corrected but no individual medicine was being promoted here. The strapline "Over 50 years experience in the management of epilepsy" was a corporate advertising statement and it was incorrect for Janssen-Cilag to consider it a therapeutic claim. Clause 4.1 required prescribing information "in all promotional material for a medicine". This advertisement was not promotional material for a medicine and was therefore not in breach of Clause 4.1.

The guidelines on company procedures stated that where format and size were different there should be a unique code for each item. It did not state format or size and this was a guideline and not a regulation. Parke Davis' Standard Operating Procedures considered it acceptable to have the same code for different size items of the same format as long as all items were reviewed and authorised by the signatories. Items of different formats were all given different codes, irrespective of size and they were individually reviewed and certified. These items were of the same format and had the same code; there was most definitely no breach of Clause 14.

Extensive and careful consideration had been put behind this advertising. This activity had resulted only in positive remarks from a number of doctors and other pharmaceutical companies at this stage and there had been no negative feedback or concern expressed to Parke Davis whatsoever.

Finally, Parke Davis regretted that it had felt forced to react so strongly and it was not intending to repeat such a campaign each time it had a Code of Practice dispute. It believed the circumstances this time to be unique and worthy of wide correction. The expense involved would not encourage such action unless doctors had been deliberately misled in a sensitive area of serious medicine.

PANEL RULING

The Panel first considered whether the advertisement came within the scope of the Code. It noted that Parke Davis claimed that the advertisement was not promotional for its product Neurontin (gabapentin). Three products were referred to in the advertisement by generic name, lamotrigine, gabapentin and topiramate. The Panel noted that the advertisement included both a product name, gabapentin, and an indication "refractory partial epilepsy". The Panel concluded that the advertisement was a form of promotion of gabapentin and was therefore within the scope of the Code. The Panel noted that even if the advertisement had only reproduced the ruling it would still have been subject to the Code in that it made critical comment about the promotion of a competitor product. The Panel considered that prescribing information for Neurontin should have been included and accordingly ruled a breach of Clause 4.1 of the Code. The Code did not recognise the concept of corrective advertisements as a special category which did not need prescribing information.

In relation to the allegation that there could not be adequate certificates for the two sizes of the advertisement, the Panel had requested Parke Davis to provide the relevant certificate, or certificates. The Panel noted that there was a single certificate headed Neurontin with the description "Topiramate Response Ad (Both Sizes)". The Panel considered that this was an adequate certificate for the purposes of Clause 14 and, in consequence, there had been no breach in that regard.

As far as the guidelines on company procedures relating to the Code were concerned, the Panel did not accept Parke Davis' interpretation that only where both format and size were different should there be a unique code number for each item. The guidelines stated "Different sizes and different layouts of a piece of promotional material should be separately certified and each should have its own unique reference number" (page 37 of the Code - Paragraph 1). Parke Davis had not followed this guidance. The guidelines did not, however, form part of the Code. They merely set out guidance on what represented good practice. The essential issue under the Code was whether or not a particular item had been certified. The Panel considered that Parke Davis would be well advised to certify different sizes of advertisements separately in the future as, on occasion, problems had arisen because of failure to do so.

Turning to the question of the concept of the advertisement, that was to say making use of rulings on Code of Practice complaints in promotional material, the Panel did not consider that this was barred by the Code. Decisions on completed cases were in the public domain, being published in the Code of Practice Review which was issued quarterly by the Authority and was available to anyone. It seemed to the Panel to be an unwarranted limitation on freedom of speech to say that, as a matter of principle, use could not be made of Code of Practice rulings in promotional material, particularly in a case like this where a company considered that its interests had been damaged by activities of another which had been ruled to have breached the Code. At the present time case reports were not usually reported in medical publications and therefore the medical profession knew little, if anything, about them. It was difficult to see why reference to published cases in promotional material should in itself be held to bring the industry into disrepute.

The Panel noted that if the industry wanted to prevent reference being made to Code of Practice rulings in promotional material, then consideration would have to be given to amending the Code to specifically prevent such use.

The Panel observed that the Parke Davis journal advertisement had attracted a lot of attention. The advertisement would be seen by a wider audience than the recipients of the Janssen-Cilag material.

Clearly, even if this type of advertising was regarded as not unacceptable in principle, it could still be in breach of the Code because of the method of execution. The advertisement in question was consistent with the case report published by the Authority but Parke Davis was open to criticism for underlining the word "misleading" in the quotation from the case report. If a statement was to be claimed to be a quotation, placed within quotation marks and with a reference, then it must appear exactly as in the original, without being modified by underlining or other such additions.

The Panel was concerned about the use of the words

"Caveat Emptor" at the top of the advertisement which it considered to be an unwarranted embellishment. "Caveat Emptor" was usually interpreted as "let the buyer beware". The Collins English Dictionary (Second Edition) stated that it was "the principle that the buyer must bear the risks for the quality of goods purchased ....". Topamax (topiramate) was a licensed medicine and the breach of Clause 7.2 of the Code which had been ruled, and which had been referred to in the advertisement, related solely to the fact that it had been inappropriate to use data from different studies in a single, comparative table included in a product monograph as the data were not from studies directly comparing the products, although that impression had been given.

The Panel considered that use of the term "Caveat Emptor" was disparaging and ruled that there had been a breach of Clause 8.1 of the Code.

The Panel considered that in the light of its comments about the inaccurate quotation and the use of the term "Caveat Emptor", Parke Davis had failed to maintain a high standard. A breach of Clause 9.1 was ruled.

The Panel did not consider that this case warranted a ruling of a breach of Clause 2 which was a sign of particular censure and was reserved for such circumstances. No breach of Clause 2 was ruled.

APPEAL BY PARKE DAVIS

Parke Davis appealed against the Panel's ruling of breaches of Clauses 4.1, 8.1 and 9.1 on three grounds.

1 The advertisement was not "promotional" in any way for a specific medicine and, indeed, could be considered to fall within the exclusions contained in the Code (Clauses 1.1 and 1.2).

2 The advertisement did not disparage "the medicines, products or activities" of Janssen-Cilag (Clause 8.1).

3 No reasonable person on the facts of the case could properly hold that the advertisement failed "to recognise the special nature of medicines and the professional standing of the audience to which they were directed". Neither could it be suggested that the advertisements could cause "offence" or that any reasonable person could properly hold that the advertisements failed to maintain high standards (Clause 9.1).

Parke Davis reiterated that its sole intention had been to point out to doctors that misleading information had been communicated to them.

Parke Davis never doubted that the advertisement would fall within the scope of the Code purely because of the critical comment on Janssen-Cilag's promotion but not for any other reason. It was approved with this in mind. Parke Davis did, however, strongly contend that the advertisement was not promotional for any medicine in the true sense of the Code, as it did not promote the prescription, supply, sale or administration of any medicine. This contention was made on two grounds.

Firstly, the advertisement appeared to fall clearly within the terms of the second exception to the term "promotion" set out in Clause 1.2 of the Code. The purpose of the advertisement was to provide a "factual, accurate and informative announcement" relating to a misleading comparison in the topiramate monograph and the ruling made by the Authority to this effect. No product claim was made; refractory partial epilepsy was mentioned only as an example to distinguish a patient group. Thus it fell squarely into this second exception.

Secondly, Parke Davis believed that no reasonable person reading the advertisement could hold that it was "promotional" for Neurontin. Parke Davis accepted that the term "refractory partial epilepsy" was mentioned as were a number of anti-epileptic agents, including gabapentin, but these were all necessary inclusions in describing the claims being corrected. Partial epilepsy was only mentioned as an illustrative example of a patient group in which particular care must be taken when making clinical comparisons. No specific connection or claim was made between this example and the products gabapentin, lamotrigine and topiramate which were mentioned in a separate paragraph. This item, when judged individually, did not promote a specific medication.

Parke Davis' second ground for appeal related to the Panel's decision to rule the advertisement in breach of Clause 8.1. Parke Davis contended that the term "Caveat Emptor" was appropriately used in this instance. This was by no means disparaging but represented a critical comment which could be substantiated. The definition referred to by the Panel and taken from the Collins English Dictionary included additional comment for explanation which was beyond the basic meaning of the term. This description was too specific to be applied in this instance as if it were the only possible use for the term "Caveat Emptor". The Concise Oxford Dictionary definition of "Caveat Emptor", for example, identified the meaning as "let the buyer beware" (this was the accurate translation from Latin) and the additional information stated "he alone is responsible if he is disappointed". The use of the expression here did not make implications about the quality of topiramate, the product, but simply stated that the buyer (in this case, the reader) must beware. This was the everyday understanding of the expression and was entirely applicable in this instance since physicians were being warned to be wary of expectations they might have as a direct consequence of reading this misleading presentation of clinical trial data.

Further, "Caveat Emptor" was, of course, a common law maxim. Since no guarantees existed surrounding these clinical comparisons, as a matter of law, "Caveat Emptor" was applicable in this instance. That being the case, it was entirely right for Parke Davis to use the term "Caveat Emptor" at the top of the advertisement.

The Panel had ruled a breach of Clause 9.1 based on the use of "Caveat Emptor" and use of underlining in the quotation. For the purpose of the advertisement the underlining was intended to denote emphasis, but Parke Davis accepted that, as this was a quotation, this addition should have been qualified.

Notwithstanding this, Parke Davis did not accept the Panel's decision to find these advertisements in breach of Clause 9.1 of the Code. The previous comments firmly substantiated use of the expression "Caveat Emptor", so the suggestion of a breach of Clause 9.1 now rested only on the use of underlining when formatting this quotation in the advertisement. If this were ruled in breach of

Clause 9.1 of the Code, the clause would be being used so broadly that every advertisement with a typographical error might have to be ruled as failing to maintain high standards. Clause 9.1 referred to having respect for the special nature of medicines and the professional audience to which the material is directed; it was intended to prevent "tasteless" advertising and promotional methods as was carefully described in the supplementary information. Parke Davis was not aware of any professional audience that has been offended by or complained about these advertisements; to its knowledge Janssen-Cilag was the only such party and it was not the intended target covered by this section of the Code. The advertisements should not be considered in breach of Clause 9.1 on the basis of the underlining, the use of the expression "Caveat Emptor", or, indeed, both of these. The advertisements did recognise the special standing of the audience to which they were directed and, far from being in breach of Clause 9.1, the advertisements in question were themselves a recognition of the responsibility of the pharmaceutical industry to prescribing physicians.

APPEAL BY JANSSEN-CILAG

Janssen-Cilag said that its original allegation of a Clause 2 breach did not relate to the principle of reference to Code of Practice decisions in promotional material but to the advertisement in its entirety. By this, Janssen-Cilag meant that the advertisement was so unsuitable and in such bad taste as to merit especial censure.

Further, regard had to be taken to the distribution of the advertisement versus the distribution of the original Janssen-Cilag product monograph. The advertisement had appeared almost weekly in the BMJ and Hospital Doctor, usually in a very prominent location. The product monograph was only issued to doctors with an interest in epilepsy and to other associated health professionals such as drug information pharmacists and hospital pharmacists. Surely any attempt at correction by Parke Davis should have been restricted to the same audience?

Additionally, the breach ruled by the Appeal Board in Cases AUTH/378/11/95 and AUTH/391/1/96 was one which was not clear cut in that the Panel ruled no breach, with this ruling being overturned at appeal. This suggested that it was not such a heinous breach as to warrant such a public attempt at correction and that there were clearly differences of opinion on this particular item within two groups of people who had extensive experience in this field.

The choice of title for the advertisement, "Caveat Emptor", deserved especial condemnation and surely was a discredit to and reduced confidence in the industry. This was a well recognised legal phrase meaning "let the buyer beware" and interpreted (Concise Oxford Dictionary 1982) as "the buyer alone is responsible if the buyer is disappointed". Janssen-Cilag contended that doctors reading Parke Davis' advice would interpret this to mean that the industry generally, and Janssen-Cilag in particular, was never to be trusted in what it said.

RESPONSE FROM PARKE DAVIS

In respect of the distribution of this advertisement versus the distribution of the original Janssen-Cilag product monograph, Parke Davis said that it was important to consider the duration of exposure as well as the location. Parke Davis had always been disturbed by what it considered the unsound action of Janssen-Cilag in the promotion of topiramate and felt it was appropriate for it, with its long history in field of epilepsy, to redress the balance.

For a full year the misleading representation had been freely available to any health professional who should request a product monograph or found themselves approached by a representative from Janssen-Cilag. It was important to note here that, in Parke Davis' view, Janssen-Cilag representatives were actively using this misinterpretation at every opportunity they had with clinicians. This kind of exposure far outstripped the level of exposure afforded by Parke Davis' announcements in the medical press over a period of a few weeks. It was wholly unreasonable to suggest that the published correction could be too broad when one considered the protracted course and nature of Janssen-Cilag's misrepresentation.

With regard to the healthcare professionals to whom the information was distributed by Janssen-Cilag, Janssen-Cilag had given Parke Davis new information. From the target audience mentioned there would, of course, be an extensive network developing. Drug information pharmacists for instance were an extremely important information source for all physicians in contact with them. This target alone would produce rapidly growing exposure to multitudes of doctors. Parke Davis' corrective advertising needed to be addressed to neurologists, general physicians, psychiatrists, paediatricians to name but a few examples of specialists who might have an interest in epilepsy. For these reasons its placement in the British Medical Journal and Hospital Doctor was entirely appropriate.

In consideration of Janssen-Cilag's comments that "there are clearly differences of opinion on this particular item within two groups of people who have extensive experience in this field", Parke Davis was surprised that Janssen-Cilag should wish to question the value of the Appeal Board's final decision. The Appeal Board had access not only to the full facts presented to the Panel but were also privy to further information presented by both companies. The allegations were researched in greater depth for the Appeal Board in order that their decision could be final. Janssen-Cilag's use of the word "heinous" was sensationalist and attempted to distract attention from the true nature and implications of the breach. The fact of the matter was that this misinterpretation was found in breach by the Appeal Board giving due consideration to all of the opinions expressed including that of the Panel. In addition, for reasons which have been given in Parke Davis' appeal, Janssen-Cilag's product monograph breach was so serious as to warrant the correction which Parke Davis applied.

Only now did Janssen-Cilag wish to draw attention to the use of "Caveat Emptor". This issue had already been addressed in detail in Parke Davis' appeal letter. The suggestion that this expression should imply that the

industry generally, and Janssen-Cilag in particular, was never to be trusted in what it said, represented exaggeration in the extreme. Janssen-Cilag itself defined "Caveat Emptor" and must surely recognise that misleading data could and would lead to expectations which could not, by definition, be fulfilled. "Caveat Emptor" was entirely appropriate here and the inference that the industry, or Janssen-Cilag in particular, was never to be trusted could not be drawn based on the specific and well defined information presented with this statement. Janssen-Cilag's inference was artificial and tortuous and Parke Davis did nothing to damage its name or that of the pharmaceutical industry.

In summary, despite Parke Davis' continued efforts to resolve its concerns in a professional manner with Janssen-Cilag over a period of nearly a year it continued to expose material which it had conceded to be in breach of the Code. It continued to maximise this exposure with all of the resources available to it. The brief spell of advertising to announce a correction was important to clinical practice and therefore in the public interest. The exposure generated by Janssen-Cilag over the previous 12 months and furthermore the method of announcement was carefully considered, appropriately distributed and not disparaging. It was a clear cut and valid critical comment, based on an Authority ruling which was provided in full. This activity could not be considered a breach of Clause 2 of the Code.

FURTHER COMMENTS FROM JANSSEN-CILAG

Janssen-Cilag said that Parke Davis made a great play of, in its opinion, Janssen-Cilag continuing to expose material which it had conceded to be in breach of the Code. This was not true.

Janssen-Cilag did acknowledge (Case AUTH/389/1/96) that there were no direct comparative data between topiramate and gabapentin but had not given any blanket undertaking never to use indirect comparisons of the respective products in the future.

The form and presentation of the indirect comparison made in the Topamax monograph, which was a fresh promotional item, were quite different from the earlier piece and this, in Janssen-Cilag's view at the time, was a valid comparison. This comparison was ruled to be valid by the Panel, a decision which was overturned upon Appeal. The company accepted this final decision and withdrew the piece in question promptly.

APPEAL BOARD RULING

The Appeal Board considered that the advertisement was clearly promotional in nature and that prescribing information for Parke Davis' product Neurontin (gabapentin) should accordingly have been included. It had not been given. The Appeal Board therefore upheld the Panel's ruling of a breach of Clause 4.1. Parke Davis' appeal failed on that point.

In relation to the general principle of whether promotional material could refer to rulings under the Code of Practice, the Appeal Board was of the opinion that this was not in itself contrary to the Code. Clearly the way in which it was done could breach the Code and the Appeal Board considered that in such advertisements great care must be taken to ensure fairness and exactitude.

The Appeal Board considered that a number of aspects of the advertisement were unacceptable, these being the use of the headline "Caveat Emptor", the use of the chalk and cheese illustration and the underlining of the word "misleading" in the quotation from the Code of Practice Review. Taking the advertisement as a whole, the Appeal Board decided that it was disparaging of Janssen-Cilag and its product, Topamax. The advertisement failed to maintain a high standard. The Appeal Board therefore ruled there had been breaches of Clauses 8.1 and 9.1 of the Code. The Panel's rulings were upheld and Parke Davis' appeal failed on these points.

The Appeal Board considered that the advertisement had brought discredit upon the pharmaceutical industry and ruled that there had been a breach of Clause 2. The Panel's ruling was overturned and Janssen-Cilag's appeal on this point accordingly succeeded.

Complaint received **5 July 1996**

Case completed **1 October 1996**

CASE AUTH/443/7/96

CIBA v GLAXO WELLCOME

Serevent leavepiece

Ciba complained about a leavepiece entitled "Serevent - a comparison with eformoterol" which had been issued by Allen & Hanburys. The leavepiece featured a table which compared the data sheet interactions/precautions of the two products.

The Panel ruled that the leavepiece was misleading as it gave the impression that eformoterol was associated with a number of known interactions/precautions whilst Serevent was associated with only one. The table listed one interaction for Serevent. While a number of interactions were listed for eformoterol Allen & Hanburys had failed to quote the data sheet statement that most of these were theoretical only, based on pharmacological first principles. The data sheet precautions, which were common to both products, were not included in the table at all but given as a footnote at the bottom of the piece.

COMPLAINT

Ciba Pharmaceuticals complained about an A4 leavepiece issued by Allen & Hanburys and headed "Serevent - a comparison with eformoterol". The leavepiece was available for representatives to request and use with GPs. The front of the leavepiece presented, in tabular form, a "Comparison of data sheet interactions/precautions" for the two products. Only β-blockers was listed for Serevent. In the eformoterol column β-blockers, digitalis, quinidine, disopyramide, procainamide, phenothiazines, antihistamines, tricyclic antidepressants, sympathomimetic agents and MAOIs were listed.

Below the comparison table were three stab points the first of which read "Serevent therapy is associated with fewer known drug interactions than efomoterol". At the bottom of the page the statement, "Concomitant treatment with xanthine derivatives, steroids or diuretics may potentiate a possible hypokalaemia effect of β-agonists" appeared in the same print size as the table but smaller than the stab points below the table.

Ciba alleged that the leavepiece was in breach of Clause 7.2 and 7.3 of the Code and raised two issues.

1 Inaccurate reflection of data sheets

Ciba alleged that the table showed an inadequate comparison of interactions and precautions listed in the Serevent data sheet and the Foradil (eformoterol) summary of product characteristics (SPC). Apart from the medicines listed in the Foradil section, three other medicines were listed under the precaution sections of both data sheets, but these were omitted from the table, appearing in small print at the very bottom of the page. The table would indicate that the Serevent data sheet listed only one possible interaction, which was not the case. Glaxo Wellcome had agreed with this point but had not withdrawn the item as requested.

2 The claim "Serevent therapy is associated with fewer known drug interactions than eformoterol"

Ciba pointed out that the claim was referenced to "Data Sheet 1995". The leavepiece claimed that the listed interactions shown in the Foradil SPC were "known" rather than theoretical. This was not the case. The published literature and Ciba's own safety database revealed only one known interaction: of high dose Foradil with a xanthine derivative. With the other products listed in the SPC the possibility of the interaction was theoretical only (for example, where a product may have a similar adverse effect to that of the β2-agonist, the two could theoretically interact by having an additive effect). Indeed, the interaction section (4.5) of the Foradil SPC began: "There are no clinical data to support the advice given below, but from consideration of first principles one might expect the following interactions:".

Glaxo Wellcome's justification was set out in a letter to Ciba, its argument was complex and required some explanation. Ciba's interpretation of Glaxo Wellcome's comments was as follows:

- Many of the products listed (in the table of interactions under the eformoterol heading) could have undesirable cardiovascular effects (it was Ciba's understanding that these cardiovascular effects were thought to be caused by activity of these drugs at the β1-receptor).
- All β2-agonists including Foradil and Serevent had the potential to cause similar cardiovascular effects at high doses. If the β2-agonist was given along with a medicine which had the similar effect, it was possible that these cardiovascular effects were additive.
- It was well accepted that all β2-agonists had some activity at the β1- and β3-receptors.
- Glaxo Wellcome was making the assumption that all the cardiovascular effects of β2-agonists were caused by their activity at β1-receptors.
- By claiming that Foradil was less selective for the β2-receptor compared to the β1-receptor than Serevent, Glaxo Wellcome was implying that Foradil had more β1 activity than Serevent, suggesting that Foradil had greater potential to interact with the products listed in the table than Serevent.
- Furthermore, Glaxo Wellcome implied that the licensing authorities may have influenced the listing of interactions in the Foradil SPC.

Ciba's comments on these arguments were as follows:-

- Ciba's decision to warn medical professionals of all potential and theoretical interactions of the class of β2-agonists in the Foradil SPC was entirely voluntary, and not influenced by the licensing authorities.
- Both Foradil and Serevent were regarded to be highly selective to the β2-receptor. There was no evidence that

any difference in selectivity had any clinical implications.

- Furthermore selectivity was only one indicator of the activity of a product at a receptor. The effect of Foradil on β1-receptors was governed by other factors, such as potency and affinity. In this case the selectivity ratio used alone was not an accurate indicator of the effect on β2-receptors.
- Glaxo Wellcome's assumption that all the cardiovascular effects of β2-agonists were caused by activity at the β1-receptor was not supported by the published literature. The only references Ciba could source on this subject speculated that this effect of β2-agonists might in fact be caused by activity at β2-receptors outside the lung such as stimulation of cardiac β2-receptors.
- Available evidence did not support Glaxo Wellcome's claims that Foradil had any greater potential to interact with the products listed in the table than did Serevent.

A number of papers were provided to support Ciba's comments.

RESPONSE

1 Inaccurate reflection of data sheets

Glaxo Wellcome said that Ciba commented that three products were listed under the precautions sections of both data sheets which Glaxo Wellcome had omitted from the table but put in "small print" at the very bottom of the page. This print was exactly the same font as appeared in the table and it quite clearly pointed out that the products concerned (xanthine derivatives, steroids or diuretics) might potentiate a possible hypokalaemic effect of beta agonists. This indicated a class effect and implied beta agonists, of which Serevent and eformoterol were just two.

This warning appeared in the Foradil SPC and in the data sheet for Serevent. Glaxo Wellcome specifically separated out this effect as it had a different mechanism of action from the beta blockers featured in both columns which competitively bound with the beta receptor.

Glaxo Wellcome referred to Ciba's view that Glaxo Wellcome had agreed with the point that the table provided an inadequate comparison of interactions and precautions listed. This was most certainly not the case. In a letter to Ciba, Glaxo Wellcome had said that "We accept that an alternative layout would be to include these precautions in both columns as you suggest". This quite clearly did not indicate that Glaxo Wellcome agreed with Ciba's contention. Glaxo Wellcome's subsequent letter to Ciba indicated "We are quite prepared to accept your request that we include "xanthine derivatives, steroids or diuretics may potentiate a possible hypokalaemic effect of beta agonists" under both Serevent and eformoterol and if we decide to reprint the item we will indeed include these items under both columns as you requested". Another letter from Glaxo Wellcome to Ciba commented "The format of the tabulation was meant to define direct drug interactions in comparison with indirect ie via hypokalaemia, and until you raised the point any problems were not perceived". This letter went on to clarify why Glaxo Wellcome had agreed to change it should the item be reprinted, Glaxo Wellcome's agreement being an attempt to "keep the peace". Glaxo Wellcome was therefore most unhappy that Ciba alleged that it had agreed that the leavepiece was misleading while not being prepared to withdraw it.

2 Claim "Serevent therapy is associated with fewer known drug interactions than eformoterol"

Glaxo Wellcome said that Ciba was obviously unhappy about the above claim which appeared as the first stab point beneath the table and in particular about the use of the word "known". Quite clearly Glaxo Wellcome's intention was to reflect the data sheets and the known, ie predictable, interactions. This was in contrast to the unknown idiosyncratic or unpredictable reactions. While Glaxo Wellcome accepted that Ciba maintained there was no clinical data to support the advice, nevertheless, Ciba did give the advice that one might expect interactions with the following products. These warnings, whether based on first principles, or clinical practice, did not appear in the Serevent data sheet.

Serevent (salmeterol) had had considerable attention paid to it, having been the first inhaled long-acting bronchodilator on the UK market. Two large post marketing surveillance studies had monitored safety and adverse events and had confirmed the tolerability of Serevent over prolonged periods of time. Glaxo Wellcome was unaware of any similar large scale safety work being carried out with eformoterol. While obviously not specifically excluding the possibility of unforeseen or foreseen (from first principles) interactions, it did emphasise the tolerability of salmeterol in clinical practice.

Glaxo Wellcome then referred to the points raised in correspondence between the two companies.

"Many of the drugs listed (in the table of interactions under the Foradil heading) can have undesirable cardiovascular effects ..."

Glaxo Wellcome would agree that some of the undesirable cardiovascular effects of the products listed were thought to be mediated by β1-receptor activity. Ciba later speculated that the cardiovascular effects of the β2-agonists were not caused by activity at the β1-receptor but by their effect on cardiac β2-receptors. This was a complex area, not least because after Lands typed the various β-receptors it was subsequently found that β2 represented 10% of beta cardiac receptors (although other authors put the proportion higher, even 40% in the ventricle and 55% in the atrium) and were responsible for both inotropic (strength of contraction) and chronotropic (rate of contraction) activity. In contrast, the β2-receptors on peripheral vasculature mediated vasodilation, a reflex release of catecholamines by the adrenal gland, causing β1-cardiac stimulation, an inotropic response and a corresponding rise in cardiac output to correct hypotension.

"All β2-agonists, including Foradil and Serevent, had the potential to cause similar cardiovascular effects at high doses."

Glaxo Wellcome submitted that cardiovascular adverse

events of beta receptors could be divided into β2-adrenoceptor mediated (including hypokalaemia and ECG changes) and heart rate, which appeared to be the result of direct stimulation of both β1 and β2-adrenoceptors. In terms of selectivity for the β2-receptor, Serevent *in vitro* had the highest selectivity of any currently available β2-agonists.

However, even Ciba's own work demonstrated dose-dependent effects on cardiovascular and metabolic parameters of eformoterol with the effect at the highest doses being of possible clinical significance. These represented single daily doses of 48 or 96 micrograms of eformoterol. This was compared with the cardiovascular effect of salmeterol which had been extensively studied by Professor Tattersfield and co-workers at Nottingham, which demonstrated that Serevent at single doses of 100-400 micrograms (ie above the licensed range) compared to salbutamol 600-2400 micrograms both caused dose dependent changes in heart rate QTc interval and potassium and glucose concentrations but at these doses systolic and diastolic blood pressure were unchanged with salmeterol. Salmeterol had slower onset and prolonged action in increasing heart rate and alterations to potassium and glucose concentrations.

In a further six month study done in this group the salmeterol group had similar PD_{20} (the dose of various inhaled spasmogens which cause a 20% fall in lung function, which therefore measures bronchial hyperresponsiveness) to metacholine, exacerbation rates and oral steroid use as the placebo group over six months.

In 1988 Serevent was shown to have minimal effect on the cardiovascular system with heart rate increasing only with salmeterol 200 micrograms as a single dose at two hours after dosing. In a previous letter Ciba suggested that there were unspecified cardiovascular events associated with salmeterol about which Glaxo Wellcome was awaiting further clarification. Obviously if Ciba had knowledge of further cardiovascular events for salmeterol then Glaxo should certainly be in possession of that information.

Muller also showed dose-dependent increase on heart rate with eformoterol in healthy volunteers (between doses of 6 and 48 micrograms) and Maesen and Smeets showed increasing pulse rate with eformoterol 48 micrograms. Over longer periods of time Midgren found more side effects with eformoterol 24 micrograms bd than salmeterol 400 micrograms bd (these were particularly palpitations and cramps). Arvidsson *et al* reported ten out of fifteen patients experiencing side effects on eformoterol 12 micrograms bd over 12 months.

"It was well accepted that all β2-agonists had some activity at the β1 and β3-receptors".

Over the last 15-20 years progress had been achieved by developing more selective β2-agonists. Ciba seemed to question much of the historical data about asthma fatalities related to the non-selective isoprenaline inhalers and the subsequent surge in mortality, in New Zealand in particular, related to fenoterol.

Serevent would seem to be 85,000 times more selective at the β2 to β1-receptors than isoprenaline whereas eformoterol was only 120 times, significantly less than salbutamol at 1375 (Johnson *et al* 1993).

Glaxo Wellcome was making the assumption that all the cardiovascular effects of β2-agonists were caused by their activity at β1-receptors".

Eformoterol certainly had greater potency than Serevent at the β2-receptor. Both, however, showed concentration related relaxant responses using isolated preparations of airway smooth muscle from both animal and man.

For an agonist to activate a receptor it must have an affinity for that receptor. The affinity determined the degree of binding of the agonist to the receptor. *In vitro* binding studies of rat lung membrane showed that Serevent and eformoterol had similar affinities, both 30-50 fold higher than that for salbutamol.

The receptor efficacy reflected the ability of a medicine to have an agonist effect at that receptor. The efficacy of Serevent at β1-receptors was very low and low also at the β2-receptor. As the potency was a product of affinity and efficacy and eformoterol was much more potent with the same affinity, it followed that it must have a greater efficacy than Serevent at both β1 and β2-receptors. This had been shown directly in tissue preparations (Johnson *et al* 1993). Selectivity data was based on functional response and not just laboratory binding affinities and therefore due to the greater potency and much reduced selectivity for eformoterol there was increasing potential for cardiovascular effects with this drug because of the efficacy difference at β1 and β2-receptors. While Glaxo Wellcome maintained that Serevent had negligible β1-receptor activity, any cardiovascular effects it suggested were mediated by the β2-adrenoceptor and only indirectly through the β1-receptor. Glaxo Wellcome suspected that, in eformoterol's case, some of the cardiovascular effects might indeed be caused by its direct activity at the β1-receptor.

These theoretical considerations for salmeterol had been borne out in practice where in some trials very careful ECG monitoring had occurred showing no increase in supraventricular or ventricular ectopic beats, pulse rate or blood pressure compared to salbutamol.

"Furthermore, Glaxo Wellcome implied that the licensing authorities may have influenced the listing of interactions in the Foradil SPC"

There was no suggestion in any of Glaxo Wellcome's letters that it believed the licensing authority might have influenced the listing of interactions in the Foradil SPC. This was obviously a matter between the licensing authority and Ciba. Glaxo Wellcome was not privy to the discussions nor would it ever imply that it was.

"Ciba's decision to warn medical professionals of all potential and theoretical drug interactions of the class of β2-agonists in the Foradil SPC was entirely voluntary, and not influenced by the licensing authorities".

Whether this was voluntary or requested by the licensing authority seemed irrelevant. The interactions were there and the medical profession had been warned. Glaxo Wellcome said it was quite justifiable to bring this warning to the attention of the medical profession.

"Both Foradil and Serevent were regarded to be highly selective to the β2-receptor. There was no evidence that any difference in selectivity had any clinical implications".

Glaxo Wellcome pointed out again that Foradil and Serevent were selective β2-receptor agonists but their degree of selectivity was very different. While it was unclear whether any difference in selectivity had clinical implications, there was potential nevertheless for such a difference in selectivity to be important.

"Furthermore selectivity was only one indicator of the activity of a drug at a receptor. The effect of Foradil on β1-receptors was governed by other factors, such as potency and affinity. In this case the selectivity ratio used alone was not an accurate indicator of the effect on β1-receptors".

Glaxo Wellcome agreed with Ciba that selectivity was only one indicator of the activity of a drug. Potency and affinity were also important and, as previously mentioned, whereas isoprenaline had a binding affinity of 200 Ki, eformoterol had an affinity of 76 and salmeterol 53. By comparing potency and efficacy it was possible to derive functional selectivity ratios for beta agonists, which Glaxo Wellcome believed was of more use than binding affinity and it was this functional selectivity that was so much greater for Serevent at the β2 to β1-receptors than that seen with eformoterol.

In summary Glaxo maintained that the leavepiece was a fair, accurate and balanced look at the relative merits of the two drugs. Six thousand copies were produced and 90% of these had now been issued. The table could have been designed in many ways, and while Glaxo Wellcome did not agree (and never had agreed) with Ciba that the particular format was misleading, nevertheless, it was prepared to change it to one which Ciba found acceptable, should it reprint the item, in an attempt to generate goodwill.

RULING

The Panel noted that the title of the table was "Comparison of data sheet interactions/precautions". The section of the Foradil SPC dealing with interactions (4.5) first stated that "There are no clinical data to support the advice given below, but from consideration of first principles one might expect the following interactions:". The SPC then listed quinidine, disopyramide, procainamide, phenothiazines, antihistamines and tricyclic antidepressants as being associated with QT interval prolongation and an increased risk of ventricular arrhythmia. It went on to state that the concomitant administration of other sympathomimetic agents may potentiate the undesirable effects of Foradil and that use of Foradil in patients being treated with MAOIs or tricyclic antidepressants should be performed with caution. The statement referring to the fact that concomitant treatment with xanthine derivatives, steroids or diuretics may potentiate a possible hypokalaemic effect of β-agonists then appeared (as given on the bottom of the leavepiece). This was followed by a statement that hypokalaemia may increase susceptibility to cardiac arrhythmias in patients treated with digitalis. The final paragraph warned about the concomitant use of β-adrenergic blockers. The Panel noted that all of these medicaments were listed on the leavepiece.

The interactions section of the Serevent data sheet stated that β-blockers should be avoided. This was the only interaction with Serevent listed on the leavepiece. In the precautions section the Serevent data sheet said that "Potentially serious hypokalaemia may result from β2-agonist therapy. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids, diuretics and by hypoxia". The Panel noted that this was similar to the warning in the Foradil SPC. The information was not included in the table but appeared as a footnote at the bottom of the page.

1 Inaccurate reflection of data sheets

The Panel considered that the table was misleading as it gave the impression that only the co-administration of beta-blockers would pose a problem in patients taking Serevent. This was not true. The table purported to list interactions/precautions for each medicine but this was not so. Only the interaction with β-blockers had been included for Serevent while the cautionary advice about xanthine derivatives, steroids or diuretics appeared as a footnote at the bottom of the page. The Panel thus considered that the table was misleading due to the omission in the table itself of information about xanthine derivatives, steroids and diuretics. The Panel therefore ruled a breach of Clause 7.2 of the Code.

2 Claim "Serevent therapy is associated with fewer known drug interactions"

The Panel noted that the list of interactions which appeared on the Foradil SPC was prefaced with the statement "There are no clinical data to support the advice given below, but from consideration of first principles one might expect the following interactions". This qualification had not been given in the table. The Panel considered that the omission of this statement was compounded by the claim "Serevent therapy is associated with fewer known drug interactions", in large type immediately below the table. This gave the impression that all the products listed under eformoterol were known to interact with Foradil. This was not true. The Panel therefore considered the statement to be misleading and ruled a breach of Clause 7.2 of the Code.

Complaint received **8 July 1996**

Case completed **13 September 1996**

Case AUTH/444/7/96

JANSSEN-CILAG v PARKE DAVIS

Letter relating to previous Code of Practice rulings

Janssen-Cilag complained about a letter sent by Parke Davis to epilepsy specialists. The letter referred to published Code of Practice cases involving Janssen-Cilag. Janssen-Cilag alleged that the letter disparaged its activities, did not recognise the high standards required for the promotion of medicines and brought discredit upon the industry. It was also alleged that no prescribing information had been given for the Parke Davis product referred to in the letter.

The Panel had already decided in Case AUTH/442/7/96 that it was not a breach of the Code to refer to previous rulings under the Code, although the manner in which it was done could breach the Code. In the present case, the Panel considered that the wording of the letter was unacceptable. It disparaged Janssen-Cilag as a company, failed to maintain high standards and brought the industry into disrepute. These rulings were upheld by the Appeal Board on appeal by Parke Davis. A further breach ruled in relation to the omitted prescribing information was not appealed.

This complaint concerned a letter sent by the medical director of Parke Davis & Co Limited to epilepsy specialists on 26 June 1996. The letter was headed "Inappropriate Clinical Trial Comparisons" and related to the rulings in a number of published Code of Practice cases, AUTH/378/11/95, AUTH/389/1/96 and AUTH/391/1/96.

COMPLAINT

Janssen-Cilag Ltd alleged that the letter breached Clauses 2, 8.1 and 9.1 of the Code for the reasons given in its complaint in a previous case (AUTH/442/7/96).

In that case, Janssen-Cilag had alleged that an advertisement headed "Caveat Emptor" issued by Parke Davis, which referred to an earlier ruling in Cases AUTH/378/11/95 and AUTH/391/1/96, *inter alia* disparaged the activities of Janssen-Cilag, contrary to Clause 8.1, did not recognise the high standards required for the promotion of medicines, contrary to Clause 9.1, and brought discredit upon the industry, contrary to Clause 2. Janssen-Cilag had also referred to a letter sent to doctors which it had not seen but which it suspected would repeat the imagery and wording of the "Caveat Emptor" advertisement.

Subsequently, Janssen-Cilag had obtained a copy of the letter and now complained to the Authority about it. In addition to the allegations mentioned above, the company considered the use of the word "invidious" in the statement "It is disappointing that a situation should arise where physicians must be advised of invidious and unfair comparisons being drawn between epileptic agents" to be reprehensible and in itself in breach of Clauses 8.1 and 9.1. Insofar as it was possible to have two breaches of Clause 2 in one item, Janssen-Cilag said that the use of the word deserved the severest censure possible and alleged that it was an additional breach of Clause 2. Furthermore, Janssen-Cilag alleged that the letter promoted Epanutin but did not give the prescribing information, contrary to Clause 4.1.

RESPONSE

Parke Davis said that the purpose of this personal letter was to alert physicians to several Janssen-Cilag promotional items which contained misleading information on topiramate (Topamax). As these items included a product monograph, an item likely to be kept and referred to again and again, Parke Davis considered it important to bring this matter to the attention of epilepsy specialists. The information presented in the letter was wholly factual and related to the recent Code of Practice ruling.

Parke Davis was very disturbed by what it regarded as the unsound action of Janssen-Cilag in the promotion of topiramate and considered it was appropriate for it, with its long history in this therapeutic area, to redress the balance. Firstly, Parke Davis considered that Janssen-Cilag failed in its professional duty to carry out undertakings agreed with Parke Davis in writing following its first complaint over one year ago. Janssen-Cilag was to write to physicians about the misleading nature of Clinical Courier; instead it repeated the offending misrepresentations in the product monograph. Secondly, Parke Davis believed that Janssen-Cilag was disinclined to discuss Parke Davis' complaint regarding the product monograph and other items before it submitted it to the Authority. It appeared that Janssen-Cilag made every effort to delay responses in order to keep questionable material in use. Thirdly, it was Parke Davis' belief that Janssen-Cilag exploited every opportunity available to it through the Code of Practice system and far from "respecting the spirit of the Code" used the system to continue to promote for commercial gain while matters were being appealed. Finally, Janssen-Cilag continued to use an advertisement after signing an undertaking to immediately cease its use (Case AUTH/439/6/96).

In the letter at issue, Parke Davis simply reiterated the Authority's ruling concerning Janssen-Cilag's promotional items. The letter simply delivered information of importance to clinical practice. This was not in breach of the letter or spirit of the Code. Parke Davis considered that this was an ethical action in recognition of the company's responsibility to patients and healthcare professionals. This activity could not be considered to bring the industry into disrepute.

With regard to Janssen-Cilag's remaining allegations, Clause 4.1 stated that the prescribing information must be provided in all promotional material. However, the promotion of a medicine was any activity which promoted the prescription, supply, sale or administration of that medicine. The statement in the letter that 1996 was the Diamond Anniversary of the launch of Epanutin clearly did not promote the prescription, supply, sale or administration of Epanutin. Consequently, Clause 4.1 did not apply.

Clause 8.1 referred to the use of disparaging references to the medicines, products or activities of other pharmaceutical companies. Parke Davis submittted that the letter was accurate, balanced, fair and fully justified - as required by Clause 8.1. Parke Davis had accurately quoted the ruling.

With regard to the use of the word "invidious" which Janssen-Cilag had said was unfair and should be considered separately as a Clause 2 breach, in addition to the whole letter, Parke Davis said that in the Concise Oxford Dictionary (7th edition) the word "invidious" was defined as: "giving or likely to give offence, especially by real or seeming injustice etc".

Physicians had a right to be advised of misleading information. Parke Davis considered Janssen-Cilag's activity in this whole affair to be offensive and totally unprofessional. From the two letters provided by Parke Davis it was clear that these doctors, at least, were also offended by Janssen-Cilag's promotional activities. The Authority should also note that Parke Davis was careful in its letter to doctors to qualify the comparison as unfair and invidious, not Janssen-Cilag as a company. Parke Davis submitted that the letter fully recognised the professional standing of epilepsy specialists and was not in breach of Clause 9.1.

Parke Davis stressed that extensive and careful consideration was put behind the letter. Parke Davis considered it important that the Authority should be aware that this activity had resulted only in positive remarks from a number of doctors and other pharmaceutical companies at this stage and there had been no negative feedback or concern expressed to Parke Davis whatsoever.

Finally, as with the "Caveat Emptor" advertisement (Case AUTH/442/7/96), Parke Davis regretted that it felt forced to react so strongly and it was not intending to repeat such a campaign each time it had a Code of Practice dispute. It believed the circumstances this time to be unique and worthy of wide correction. The expense involved would not encourage such action unless doctors had been deliberately misled in a sensitive area of serious medicine. As with all antiepileptic drugs, including topiramate, usage should be evaluated on accurate facts. Parke Davis did not expect this circumstance to recur.

PANEL RULING

The Panel noted that the letter stated "Following complaints, including one from a consultant neurologist, the Association of the British Pharmaceutical Industry (ABPI) has ruled that some of the promotional items in physicians' possession have breached the ABPI Code of Practice". It was the Code of Practice Panel and the Code of Practice Appeal Board of the Prescription Medicines Code of Practice Authority which had made the rulings and not the ABPI. The Authority and the ABPI operated separately and the ABPI itself had no involvement in rulings on complaints.

The Panel considered that the letter was promotional in nature and that it thus came within the scope of the Code. The letter referred to two of Parke Davis' products, Epanutin and Neurontin. Even if the advertisement had not mentioned those products, the Panel considered that it would still have been subject to the Code in that it made critical comments about the promotion of a competitor product.

The Panel noted that the letter made a claim for gabapentin (Neurontin) and bore prescribing information for that product on its reverse. The letter also stated "Indeed, you may already be aware that 1996 is the Diamond Anniversary of the launch of our first antiepileptic agent, phenytoin (Epanutin)." The Panel noted that it was well established that any such mention of a product triggered the need for prescribing information and ruled that there had been a breach of Clause 4.1 of the Code as the prescribing information for Epanutin had not been included.

In relation to the general question of the use in promotional material of rulings on Code of Practice complaints, the Panel reaffirmed its view, as set out in its ruling in Case AUTH/442/7/96, that this was not prohibited by the Code. Although such advertising was not regarded as unacceptable in principle, it could still be in breach of the Code because of the method of execution.

The letter referred to three promotional items from Janssen-Cilag, these being a topiramate product monograph, an advertisement which had appeared in the British Medical Journal on 4 November, 1995, and a Clinical Courier symposium report entitled "Topiramate: New Advances in the Treatment of Epilepsy".

In relation to the monograph and the Clinical Courier, the letter then stated that data in the items "..... compares the efficacy of topiramate with the established antiepileptics gabapentin and lamotrigine. The implication of the data was that topiramate was superior to gabapentin and lamotrigine. With no direct comparative data for the three products it is inappropriate to attempt such a comparison and its inclusion in promotional items is wholly misleading".

The letter did not explain why the journal advertisement had been ruled to be misleading. The Panel noted that the journal advertisement had not made inappropriate comparisons with other products as suggested by the title of the letter, "Inappropriate Clinical Trial Comparisons". The ruling concerned a claim which was considered to be too general, given the licensed indications for Topamax. The Panel considered that it was unsatisfactory for such an unexplained referral to a ruling to be made.

The Panel did not wish to undermine the rulings which had been made in relation to the use of the data on the three antiepileptic products or to minimise them. The Panel considered, however, that the letter was over critical of the situation and too much was being made of it by Parke Davis. In this regard it noted the use of the expressions "Due to the serious nature of this incident ....." and "physicians must be advised of invidious and unfair comparisons .....". The language used in these expressions was particularly strong and, in the Panel's view, would give recipients of the letter a biased view of the rulings regarding the product monograph and the Clinical Courier.

Given the criticisms noted above, the Panel decided that

the letter disparaged Janssen-Cilag as a company and therefore ruled a breach of Clause 8.1 of the Code. Further, the Panel decided that Parke Davis had failed to maintain a high standard and a breach of Clause 9.1 of the Code was ruled.

The Panel considered that the tone and content of the letter amounted to a breach of Clause 2 and ruled accordingly.

APPEAL BY PARKE DAVIS

Parke Davis said that it did not agree with the Panel's decision to rule this letter in breach of Clauses 2, 8.1 and 9.1 and appealed against the Panel's decision on all of these counts. It accepted that there had been a breach of Clause 4.1.

The letter was a personal comment to doctors concisely informing them of misleading information that had been actively provided to them by Janssen-Cilag. Parke Davis' position had always been one of promoting clear and accurate scientific information. Promotional activities of another company compromised this and attempts at resolving Parke Davis' concerns directly with Janssen-Cilag had been ignored. In Parke Davis' view, Janssen-Cilag then exploited the protracted period of debate to maximise its promotional gain. Parke Davis' position on the misleading promotion by Janssen-Cilag was supported by the Appeal Board and the company considered that as clinicians would not be aware of this ruling, it was important that they should be advised accordingly. This was a difficult endeavour and Parke Davis discussed and deliberated several options. Parke Davis decided in the end on a short journal advertising campaign and a personal letter from its medical director to physicians with an interest in epilepsy. Parke Davis considered that as a number of these doctors were likely to have a copy of the topiramate product monograph on their bookshelves, such action was fully justified.

In the letter Parke Davis merely reiterated the Prescription Medicines Code of Practice Authority's ruling concerning Janssen-Cilag's promotional items. It simply delivered information of importance to clinical practice. This was not in breach of the letter or spirit of the Code, it was an ethical action in recognition of Parke Davis' primary responsibility to patients and health care professionals.

Parke Davis accepted that it did not explain why the Janssen-Cilag journal advertisement had been ruled to be misleading and on reflection it recognised that it should have done so for completeness. However, this was as a result of attempting to be clear and concise. Parke Davis did offer the opportunity to call it for any information or clarification and this would have been easily available but no enquiries were received at all. This was the first time that Parke Davis had taken action of this kind and its motive was to inform clinicians about the true facts regarding the inappropriate comparison that Janssen-Cilag had been so actively presenting to them. It was important that this fact remained at the forefront and was not lost in the detail.

The Panel had said that the letter was over critical of the situation and too much was being made of it by Parke Davis. The Panel stated that the language was strong and would give the recipients a biased view of the rulings. Parke Davis would contend that the language used was appropriate when raising this issue in the current climate of evidence based healthcare. It was difficult to convey the importance of the situation without a certain level of strength in the language and form of words. Physicians were actively seeking data on which to base prescribing decisions and Parke Davis considered that misrepresentation of clinical data was a serious matter and that these comparisons were both unfair and offensive.

Clause 8.1 referred to the use of disparaging references to the medicines, products or activities of other pharmaceutical companies. The statements Parke Davis used were, in its view, accurate and fully justifiable critical comment. There was no disparaging reference to Janssen-Cilag whatsoever. Parke Davis could not be held responsible for the fact that Janssen-Cilag was associated with this comparison. Parke Davis had been careful in its letter to doctors to qualify the comparison as unfair and invidious, not Janssen-Cilag as a company.

The letter fully recognised the professional standing of epilepsy specialists and was not in breach of Clause 9.1. This clause was intended to prevent tasteless forms of promotion as was clearly outlined in the supplementary information. The allegation of a breach of Clause 9.1 could bear no relation to the clause or this supplementary information.

The Panel had ruled that the tone and content of the letter was in breach of Clause 2 although it was unable to specify why this was considered to be the case. As this ruling was the ultimate censure, reserved for the most serious of breaches which bring discredit upon, or reduce confidence in the whole pharmaceutical industry this suggestion surely could not be upheld. It was inconceivable that this letter could reduce confidence in the pharmaceutical industry. The Code of Practice system accepted that individual doctors might be offended by some forms of promotion but this in itself did not bring Britain's pharmaceutical industry into disrepute otherwise every physician's complaint which was upheld would amount to a Clause 2 breach. There had been no complaints by healthcare professionals, the only complaint had been from Janssen-Cilag who had an obvious vested interest.

Parke Davis was not intending to repeat such a campaign in the event of a Code of Practice dispute in the future. It considered the circumstances here to be unique and worthy of wide correction.

APPEAL BOARD RULING

The Appeal Board noted that it had already determined that reference in promotional materials to the outcome of a case under the Code of Practice did not in itself amount to a breach of the Code (Case AUTH/442/7/96). The manner in which such references were used could, of course, breach the Code and high standards would be required.

The Appeal Board considered that the letter was stronger in its critical tone than was the advertisement considered in Case AUTH/442/7/96. Expressions such as "Due to the serious nature of this incident ..." and

"physicians must be advised of unfair and invidious comparisons ..." were inappropriate. Although a journal had a more visible impact the letter was more likely to be read in detail. The Appeal Board upheld the Panel's rulings that there had been breaches of Clauses 2, 8.1 and 9.1 of the Code.

The appeal accordingly failed.

Complaint received 22 July 1996

Case completed 1 October 1996

CASE AUTH/445/7/96 *NO BREACH OF THE CODE*

CONSULTANT PHYSICIAN v LEDERLE

Gastro Care Programme

A consultant physician complained about a Gastro Care Club Pack issued by Lederle to patients prescribed Zoton. The complainant questioned the ethics of inviting patients to join a patient support programme, to be on a mailing list and to receive questionnaires about their symptoms.

The Panel considered that the Gastro Care Club Pack was acceptable under the Code. The Pack was non-promotional, factual and balanced. No breach of the Code was ruled.

A consultant physician complained about a Gastro Care Club Pack issued by Lederle. The pack was presented in an A4 cardboard wallet which contained the following items: a letter headed "Welcome to the Gastro Care Club Pack"; a questionnaire (15 questions) for the patient to fill in with personal information about themselves and their condition; an envelope in which to return the questionnaire and a booklet entitled "Choices in Acid-Related Disorders" which had been written by a consultant gastroenterologist.

The Gastro Care Club was for patients taking the proton pump inhibitor lansoprazole (Zoton). In the tablet pack there was a leaflet inviting patients to join the Gastro Care Programme. The patients were then included on a mailing list and received the packs.

COMPLAINT

The complainant said that while he had no objection to the brochure on choices in acid related disorders, and the information sheet given, he thought there must be some question on the ethics of inviting patients to join a Gastro Care Programme, to be on a mailing list and to receive questionnaires about their symptoms.

RESPONSE

Wyeth Laboratories, on behalf of Lederle, submitted that the Gastro Care Programme was designed as a patient support programme which complimented the care given by the patient's general practitioner. Wyeth believed that the materials supplied to the patients enrolled in the Gastro Care Programme recognised the special nature of medicines while concentrating on matters other than the use of medicines in the treatment of acid related conditions.

The product name, Zoton, did not appear in any of the material supplied to patients. The generic name, lansoprazole, appeared in the "Choices in Acid-Related Disorders" booklet in a list of drugs alongside cimetidine, ranitidine, famotidine, nizatidine and omeprazole as examples of drugs that reduced acid production in the stomach. No attempts were made to advertise or promote Zoton, or lansoprazole in any of the materials. Therefore Wyeth considered that there was no breach of Clause 20.1 of the Code.

The only information about medicines was contained within the "Choices in Acid-Related Disorders" booklet, about which the complainant had no objection. Patients were encouraged to consult their doctor if they were unsure about anything relating to their condition or its treatment. None of the information contained in any of the materials encouraged the patient to ask their doctors to prescribe a specific medicine. Therefore, Wyeth considered that there was no breach of Clause 20.2.

The Gastro Care Programme pack was sent to the patient following the return of a completed tear-off strip attached to the patient information leaflet.

The patient information leaflet was approved for use by the Medicines Control Agency (MCA) in February 1995. All the documentation currently available in the Gastro Care Programme was seen by the MCA during this approval process.

As stated clearly in the letter to the patient, the purpose of the questionnaire was "to help Wyeth plan any further information or booklets that you may wish to receive". The results from the questionnaire were NOT to be used for any purpose other than to tailor material to the patient's needs. Further information was sent to the patient following completion of the questionnaire and was not dependent upon further prescription of Zoton. Three booklets were being developed currently. They had been written by a consultant gastroenterologist. All three were at a draft stage and were not yet approved for release.

RULING

The Panel noted that it was acceptable for companies to provide non-promotional information about prescription medicines to patients if it was factual and presented in a balanced way. The information must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of a product. Patients must not be

encouraged to ask their doctors to prescribe a specific medicine.

The Panel considered that the Gastro Care Club Pack fulfilled these requirements. The booklet "Choices in Acid-Related Disorders", discussed the medicines available but gave no more prominence to the role of lansoprazole than to that of any of the other medicines which might have been prescribed. The booklet also detailed clinical investigations which patients with reflux disease might require ie barium meal and endoscopy. This was appropriate information given the patient group which would be prescribed Zoton. The questionnaire was non-promotional and aimed only at eliciting information from the patient about their problem and how it affected their lifestyle and work. Its purpose was solely to assist in the devising of further materials to be made available to patients. The Panel noted that the MCA had seen the materials and had not objected to them.

The Panel considered that both the concept of the Gastro Care Club and the materials which were supplied were acceptable and accordingly ruled no breach of the Code.

In considering this case the Panel observed that members of the medical profession were often concerned when information was sent direct from a pharmaceutical company to their patients without their knowledge. There was no information as to what the position was in this case but, as a matter of principle, the Panel considered that doctors should be made aware of what was being offered or sent to their patients.

Complaint received **22 July 1996**

Case completed **29 August 1996**

Case AUTH/447/7/96 *NO BREACH OF THE CODE*

GENERAL PRACTITIONER v SANDOZ

Climesse journal advertisement

A general practitioner complained about an advertisement for Climesse issued by Sandoz in which the letter "i" of the word "strings" in the headline "HRT without strings" took the form of a picture of a tampon. It was alleged that this was base and offensive.

The Panel accepted that some people would find the advertisement offensive but considered that it was unlikely to cause offence to the majority of those who saw it. No breach of the Code was ruled.

This complaint concerned an advertisement for Climesse (ref CMS 96/02), issued by Sandoz Pharmaceuticals, which had appeared in a number of medical journals. The headline was "HRT without strings". The letter "i" of the word "strings" took the form of a picture of a tampon with a string hanging beneath it.

COMPLAINT

A general practitioner wrote to express her disgust at the advertisement. She thought that it was base and offensive and considered that it should be withdrawn.

RESPONSE

Sandoz Pharmaceuticals said that increased awareness of the risks of osteoporosis and the potential protection offered by hormone replacement therapy (HRT) was now encouraging more postmenopausal women to seek treatment whether or not they were still experiencing the usual menopausal symptoms. However, general practitioners were often reluctant to prescribe HRT to older women where compliance was known to be compromised by the inconvenience of the monthly period, particularly if periods had ceased naturally some time before HRT therapy was to begin.

Period free HRT, such as Climesse, which was designed to prevent stimulation of the endometrium of postmenopausal women, resulting in amenorrhoea, was thus viewed by many doctors as a new opportunity to achieve HRT protection in this patient group.

However, research had shown that faced with an extensive range of HRT options available to them, many prescribers were unable to distinguish between products or to clearly identify the relevant clinical benefits for their patients of the different products available.

The Climesse advertisement had been selected to identify clearly for prescribers the key product proposition of an HRT with no periods and thus no strings. Market research on this particular image and strapline had been received extremely positively by a panel of prescribers who considered the image to be impactful and informative rather than offensive or in bad taste. A summary of the results of this initial market research activity was provided.

In support of this initial research, Sandoz now had nearly five months experience of the use of this advertisement in the medical press since its first appearance on 12 March, 1996. During this five month period, the advertisement had received fairly comprehensive coverage in the medical press and had resulted in an estimated current awareness among general practitioners of 32% (32% of 36,000 = 11,520 general practitioners). No other complaints about the acceptability of the advertisement had been received by the company to date.

Sandoz submitted that it would be wrong to consider the content of an advertisement in bad taste simply because it used the image of a tampon when advertisements for sanitary products in general were such a feature of the lay press and media and a reference to such imagery was not received with the same embarrassment that such products elicited in the past.

It was, of course, clear that the use of such imagery must be handled with tact and care and it must be stressed that

there were no plans to elaborate on this particular theme in future promotional items or images, once the key benefits of the product had been appreciated by the prescribing audience.

Sandoz, did not consider, therefore, that the Climesse advertisement was in poor taste or that it represented in any way a breach of the Code.

RULING

The Panel noted the requirement of Clause 9.1 of the Code that all promotional materials and activities must recognise the special nature of medicines and the professional standing of the audience to which they were directed and must not be likely to cause offence.

The Panel accepted that some people would find the advertisement offensive. The Panel considered, however, that it was unlikely to cause offence to the majority of those who would see it. It was ruled that there had been no breach of Clause 9.1 of the Code.

Complaint received **31 July 1996**

Case completed **27 August 1996**

CASE AUTH 450/8/96

PFIZER v BOEHRINGER INGELHIEM

Motens detail aid

Pfizer complained about two pages in a Motens detail aid issued by Boehringer Ingelheim.

The Panel ruled that a page showing a bar chart was misleading in breach of the Code in that, despite the labelling, the bar chart conveyed the impression that there was a large difference between Motens and amiodipine in relation to vasodilator adverse events although the data were not statistically significant.

The Panel accepted the submission from Boehringer with regard to a claim that there was no evidence of a significant difference in the plasma elimination half life between young and elderly subjects. No breach was ruled.

Pfizer Limited complained about a Motens Detail Aid (ref BIL4909) issued by Boehringer Ingelheim Limited. There were two matters which were considered as follows:

1 Page headed "Shown to be well tolerated"

This page consisted of a bar chart showing the percentage of patients experiencing vasodilator adverse events while taking Motens or amlodipine. There were 40 patients in each group. 12.5% of patients experienced oedema while taking Motens compared to 27.5% of those taking amlodipine. 7.5% of patients experienced headaches while taking Motens compared to 17.5% in the amlodipine group. The p value for each comparison was 0.16. Underneath the bar chart was the claim "Helps avoid patient discomfort".

COMPLAINT

Pfizer said that the page was clearly designed to compare Motens and amlodipine. It was referenced to a study by Lombardo and Raimondi. The study used non equivalent doses of lacidipine (Motens) and amlodipine. The lacidipine dose of 4 mg was an initial dose whereas 10mg amlodipine was a high titrated dose. Pfizer pointed out that the side effects of dihydropyridines were known to be dose dependent. In addition the study was of open design. It was totally inappropriate to derive a comparison of toleration or indeed efficacy from such a study. Pfizer drew attention to the conclusion from the paper itself which was that the study "... should be considered as a pilot open-label comparative clinical experience and further experience is needed to better compare the risk-benefit profile of ... lacidipine and amlodipine". Breaches of Clauses 7.2, 7.6 and 7.7 of the Code were alleged.

RESPONSE

Boehringer Ingelheim stated that the page indicated the percentages of patients experiencing specific vasodilator adverse events, the number of patients randomised to each treatment and the lack of statistical significance in the differences between treatments (p values were 0.16). The only implication of the small scale trial of hypertensive patients treated for 8 weeks was that lacidipine was neither better nor worse than amlodipine at the doses declared. The claim "well tolerated" applied to both products. No comparative claims were made and the information was provided so as to respond to the question "do you have any data comparing lacidipine with amlodipine?". This was a reasonable question frequently put by doctors given that both medicines were prescribed once daily, being known to have a long duration of effect.

Boehringer Ingelheim submitted that the dosing issue was a distraction. The study was performed in Italy where Pfizer marketed a 10mg tablet stating that the dose was 5 to 10mg without comments as to initial dosing. There were no dose-response data comparing the relative potencies of the two products. Istin (amlodipine) in the UK had a two step titration from 5 to 10mg, Motens had a three step titration from 2 to 6mg. One could not make any inferences as to potency equivalence or non equivalence by comparing data sheets. This had been confirmed by the recent approval by the Medicines Control Agency of a summary of product characteristics (SPC) variation to the effect that all patients should receive initial dosing with Motens at 2mg.

RULING

The Panel noted that it was a well established principle

under the Code than non statistically significant data should not be presented in such a way as to give the visual impression of a substantial difference.

The Panel examined the bar charts and noted that at the top of each bar the percentage was given and the number of patients were given at the foot of each bar. The Panel considered, however, 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 the incidence of oedema and headache although this difference was not statistically significant. The p values for the differences were given on the chart but doctors would not generally appreciate that the p values of 0.16 meant that the visual differences were not statistically significant. The impression of a difference between the products was compounded by the claim "Helps avoid patient discomfort" which appeared at the bottom of the page.

The Panel noted that the study itself concluded that the study "...should be considered as a pilot open-label comparative clinical experience and further experience was needed to better compare the risk-benefit profile of ...lacidipine and amlodipine".

The Panel decided that overall the page was misleading and therefore ruled a breach of Clause 7.2 of the Code.

2 Page headed "Age-independent terminal plasma elimination half-life"

This page included the quotation "It is clear that renal and hepatic function may be impaired in the elderly, and that this may result in a steady-state drug accumulation which is greater than that in young patients" followed by the claim "This is not the case for Motens". This was followed by a bar chart comparing the mean steady-state half-life of Motens in young (15.9 hours) and elderly subjects (17.2 hours). The final statement on the page was the quotation "... there was no evidence of a significant difference in the terminal elimination half-life of (Motens) between young and elderly subjects".

COMPLAINT

Pfizer alleged that the statement "renal and hepatic function may be impaired in the elderly, and this may result in a steady-state drug accumulation which is greater than that in young patients. This is not the case for Motens" was inappropriate given that the Motens data sheet stated that the dosage should be reduced in such patients. Given that this was a safety related statement breaches of Clauses 7.2 and 7.7 were alleged.

RESPONSE

Boehringer Ingelheim said that Pfizer mistakenly alleged that the page was in breach of 7.2 and 7.7 insofar as the information presented related to the data sheet guidance on dosing. This was incorrect. The claim was that the terminal plasma elimination half-life of Motens was not significantly different in young or elderly. This was an important finding for a medicine that would be used in either population. Age dependence of plasma elimination half-life had been reported for a number of other calcium antagonists, including verapamil, nifedipine, nitrendipine and amlodipine. Boehringer said that Meredith (to whom the statement was referenced) pointed this out very clearly in his article and the information was important for prescribers seeking to avoid the possibility of accumulation. The data sheet recommended initial dosing of 2mg in the elderly to avoid an undesirable excessive fall in blood pressure and not because of a delay in plasma elimination half-life. This particular advice was now redundant in the light of the recently approved recommendation for 2mg initial dosing in all patients.

RULING

The Panel observed that the page referred to age independent terminal plasma elimination half-life. The Panel noted Boehringer Ingelheim's submission that the data sheet recommended initial dosing of 2mg in the elderly so as to avoid an undesirable excessive fall in blood pressure and not because of a difference in plasma elimination half-life. The Panel also noted that this particular advice was now redundant as the SPC recommended 2mg initial dosing in all patients. The Panel accepted the company's submission and ruled no breach of the Code.

Complaint received **2 August 1996**

Case completed **1 October 1996**

CASE AUTH/451/8/96

SMITHKLINE BEECHAM v PASTEUR MÉRIEUX MSD

Avaxim journal advertisements

SmithKline Beecham complained that the claim "And this is what helps make AVAXIM fast, painless and problem-free for you too" in Avaxim journal advertisements issued by Pasteur Mérieux MSD was misleading. The implication of the word "too" was that Avaxim was painless and problem-free for the patient but no intramuscular injection could be painless or problem-free. Further, "problem-free" was equivalent to "safe" in this context.

The Panel considered that the claim implied that Avaxim was painless and problem-free for the patient and ruled it to be misleading in view of the prescribing information which gave local pain as one of a number of possible adverse reactions and referred to the need to have appropriate treatment available in case of anaphylaxis. In the Panel's view, the claim was tantamount to saying, without qualification, that the product was safe.

COMPLAINT

SmithKline Beecham Pharmaceuticals UK complained about three journal advertisements issued by Pasteur Mérieux MSD Ltd, in respect of its hepatitis A vaccine, Avaxim (refs AX/0639/596/MSC, AX/0640/596/MSC & AX/0583/496/MSC). Each had the same text but with different visuals.

SmithKline Beecham alleged that the final sentence of the claims made in the advertisements "And this is what helps make AVAXIM fast, painless and problem-free for you too" was misleading in breach of Clause 7.2. As the advertisements were directed to healthcare professionals, the clear implication from the use of the word "too" was that Avaxim was fast, painless and problem-free for the patient. This was misleading as no intramuscular vaccine could be "painless" or "problem-free". Indeed, pain was listed as one of the adverse events in the prescribing information. Furthermore, SmithKline Beecham contended that "problem-free" was equivalent to "safe" in this context, which was in breach of Clause 7.7.

RESPONSE

Pasteur Mérieux MSD said that, as it understood it, SmithKline Beecham's objection was that it was making a claim regarding product safety issues of the vaccine as they related to the vaccinee. If this was in fact Pasteur Mérieux MSD's claim, then there would probably be justification for the complaint. This was not, however, the case. The journal advertisements were only in the medical press and therefore only healthcare professionals would see them. No vaccinee could possibly misconstrue what was being stated.

When the copy of the final part of the advertisement was considered in context, it could be seen that what was actually written was as follows:

".....Our aim is to make hepatitis A vaccination as painless and problem-free as possible for the patient.

And this is what helps make AVAXIM fast, painless and problem-free for you too."

The company submitted that in the first sentence, it was perfectly clear that there was no claim that the vaccine was painless and problem-free for the vaccinee. Only a statement that Pasteur Mérieux MSD's *aim* was to make it "as painless and problem-free as possible for the patient". When the next sentence was read in the correct context, this objective and the benefits conferred on the healthcare professionals due to the design of the product (a small volume, pre-filled syringe with a small gauge needle and a detachable label on the syringe barrel), all of which were mentioned in the previous paragraph in the advertisement, were what helped make Avaxim fast, painless and problem-free for them too. Nowhere in the text were product safety issues mentioned and adverse reactions were clearly stated in the prescribing information at the bottom of the advertisement.

RULING

The Panel noted that the claim "And this is what helps make AVAXIM fast, painless and problem-free for you too" related to benefits for the doctor. The Panel considered, however, that the claim implied that Avaxim was painless and problem-free for the patient. The Panel considered that the claim was misleading in view of the prescribing information which gave local pain as one of a number of possible adverse reactions and referred to the need to have appropriate treatment available in case of anaphylaxis. In the Panel's view the claim was tantamount to saying, without qualification, that the product was safe. Breaches of Clauses 7.2 and 7.7 were ruled.

Complaint received **5 August 1996**

Case completed **11 September 1996**

CASE AUTH/453/8/96

E MERCK v LEO

Dovonex competition poster

E Merck complained about a conference poster, used by Leo, which drew attention to a competition in which delegates were invited to show, by marking a bar chart, the relative efficacy of tacalcitol compared to that given for Dovonex. Merck alleged that the use of a question mark instead of a bar for tacalcitol was disparaging and suggested a level of efficacy for the product which could not be substantiated.

The Panel did not accept that the question mark implied a specific efficacy for tacalcitol but did consider that its use was disparaging because it implied that the efficacy of tacalcitol was in doubt. A breach of Clause 8.1 was ruled.

Merck Pharmaceuticals complained about a poster which appeared on the Leo Pharmaceuticals Limited stand at the British Association of Dermatology meeting held in July 1996. The poster drew attention to a competition in which conference delegates had to judge the efficacy of tacalcitol (Merck's product, Curatoderm) compared to that of Dovonex (Leo's product). The poster was headed "Make your mark - Dovonex vs tacalcitol - Judge the efficacy". A bar chart showed Dovonex with an efficacy of 73.2%. Instead of a bar for tacalcitol there was a question mark, the "dot" of which was bar shaped and labelled "tacalcitol". The height of this bar was less than one third of that given for Dovonex (about 15%) and the height of the question mark overall was about four fifths that of the Dovonex bar (just below 60%). The entry form for the competition reproduced the bar chart but omitted the question mark for tacalcitol. Delegates were asked to mark a cross on a vertical line labelled "tacalcitol", to show where they judged its efficacy to be. The competition prize was a personal organiser.

COMPLAINT

Merck alleged that the poster, which apparently compared the efficacy of Dovonex with tacalcitol, was in breach of Clauses 7 and 8 of the Code.

The presentation, in highlighting the efficacy of tacalcitol as a big question mark, was clearly disparaging and, further, the placing of the dot of the question mark suggested a level of efficacy which was not accurate and balanced and was obviously ambiguous. Such a comparison was not capable of substantiation. This reference to another company's product was also clearly intended to be disparaging.

RESPONSE

With regard to Merck's allegation that the presentation, in highlighting the efficacy of tacalcitol as a big question mark, was clearly disparaging and that the placing of the dot of the question mark suggested a level of efficacy which was not accurate, balanced and was obviously ambiguous, Leo submitted that it was discussing the level of efficacy of tacalcitol. There was no suggestion by Leo or by Merck that the question mark raised the issue of whether tacalcitol was efficacious. In addition, the placing of the dot of the question mark should not be interpreted as indicating the level of efficacy. The top of the question mark could equally be considered to indicate the efficacy of tacalcitol. The question mark was not intended in any way to indicate the level of efficacy.

With regard to the allegation that the question mark suggested a level of efficacy which was not accurate and balanced and was obviously ambiguous, Leo submitted that the competition raised an "open" question in respect of the relative efficacy of Dovonex and tacalcitol. The question mark was not intended in any way to indicate the level of efficacy and Leo drew attention to the competition form in this respect which included no question mark. The design of the answer form was such as not to influence the answer given in any way.

Leo said that in both the poster and competition form, the artwork, illustrations and graphs were presented in such a way as to give a clear, fair and balanced view of the matters dealt with, with no attempt to make unfair comparisons, and therefore they were not disparaging.

In respect of Merck's statement "such a comparison was not capable of substantiation" Leo pointed out that no comparative claim had been made nor implied. Leo did, in fact, have information upon which comparative claims could be made in its own promotional material. The established facts were that a comparative trial between Dovonex twice daily and tacalcitol once daily had been carried out by Nycomed in Scandinavia (the tacalcitol licensees in Scandinavia). Leo were approached by Nycomed to provide Dovonex in quantity for the purpose of this study. Under Danish law, Leo was entitled to the result of this comparison, and the efficacy and safety data for Dovonex treated patients had been provided to Leo by Nycomed. The Dovonex efficacy result stated in this competition (73.2%) was taken from the report of that study. The tacalcitol results had been made available to Leo by personal communication from one of the investigators. Leo was able to publish the Dovonex results but not the tacalcitol data. Hence, although relative efficacy of Dovonex and tacalcitol was known to Leo, at the present time, Leo did not propose to make comparative claims since it was able to publish only the Dovonex results from this trial. It was for these reasons that only Dovonex efficacy was given in the competition details. These facts were also the reason why the correct competition results could not be disclosed.

This competition was directed to dermatologists since it required a significant level of scientific knowledge and clinical expertise. Details of the scientific background were provided.

RULING

The Panel considered that the material was promotional for Dovonex and so came within the scope of the Code. The Panel did not accept that the height of the tacalcitol

question mark itself or of its "dot" implied a specific efficacy for the product. In the Panel's view, however, the question mark implied that the absolute efficacy of tacalcitol was questionable. Curatoderm was a licensed product and such critical reference was unjustified. The use of a question mark in association with tacalcitol was disparaging and the Panel ruled a breach of Clause 8.1 of the Code.

The Panel considered that while the poster had clearly disparaged tacalcitol it had not made any comparative claims in respect of the two products. The Panel ruled no breach of Clause 7 of the Code.

In consideration of this case the Panel had reservations regarding the competition as a whole and decided that the matter should be taken up with Leo under the provisions of Paragraph 16 of the Constitution and Procedure (Case AUTH/464/9/96).

Complaint received **9 August 1996**

Case completed **29 September 1996**

CASE AUTH/457/8/96 *NO BREACH OF THE CODE*

CONSULTANT PHYSICIAN v ROSEMONT

Reference to methadone in "Juice"

A consultant physician complained about the sponsorship of "Juice", a magazine for methadone users, by Rosemont. He considered that the publication glamorised and promoted the use of methadone.

The Panel considered that the publication was aimed at a very specific audience and although unusual in style and content could not be regarded as glamourising methadone use. The publication was not wholly dependent on the financial support given by Rosemont and the publisher retained full editorial control. References to Rosemont's methadone were considered to be balanced. The Panel did not accept that the magazine constituted the advertising of prescription only medicines to the general public. No breach of the Code was ruled.

This complaint concerned a publication entitled "Juice" which had the subtitle "the methadone magazine". The cover described the publication as featuring "Real life methadone stories", "Articles from top experts" and including "A message from the originator of methadone treatment - ....". Page two of the publication stated under the heading sponsorship "Financial support from Rosemont Pharmaceuticals enabled the publishers to keep the price down whilst retaining full editorial control".

When writing to Rosemont Pharmaceuticals Ltd, the Authority drew attention to the provisions of Clauses 9.1, 10.1, 20.1 and 20.2 of the Code.

COMPLAINT

A consultant physician said that the publication "Juice" was obviously aimed at glamorising and promoting the use "of a non over-the-counter medication" - methadone.

Whilst there was no doubt that the publication contained some useful health education material, the complainant did not think that anyone in their right mind could fail to come to the conclusion that the glossy presentation etc glamorised the use of methadone. The complainant personally did not think that a drug company could wash its hands of anything that it sponsored by saying that "the editor retains full control".

The complainant said that he had very mixed feelings about the publication. He was a regular prescriber of methadone for harm reduction and was gently in favour of the decriminalisation of drugs but nevertheless he had great reservations about a drug company sponsoring such publications which were obviously designed to bring their particular product to the attention of the general public. The publication said that "Competition means more choice for methadone patients" and it was interesting to note which company. The company which was sponsoring the journal, Rosemont, also made the new preparations of methadone. This might be acceptable practice for an over-the-counter medication but the complainant would be interested to hear views on this advertising vehicle for non over-the-counter medications.

RESPONSE

Referring to Clause 9.1 of the Code, Rosemont Pharmaceuticals said that it recognised that the publication "Juice" was directed at a specific group of the general public, ie, methadone users, and therefore it could not and would not wish to advertise prescription only medicines. No advertisement from Rosemont appeared in the magazine. Rosemont was identified as a sponsor and it was stated that Rosemont had no influence over the editorial content. Under the heading "Competition means more choice for methadone patients", both Martindale and Rosemont were mentioned as well as the fact that other companies (unspecified) were making Methadone DTF. Further down it stated that methadone concentrate was now available from Rosemont. The article was not written by, or amended by, Rosemont. There was no mention of Rosemont brand names nor was there any inducement for a methadone user to try to request a particular methadone from a specific company. In addition to this, the particular piece of text referred to specifically mentioned "whoever the manufacturer is, and however it tastes or looks, Methadone Mixture 1mg/1ml has the same effect". The article appeared to be balanced and factual and the reason why Rosemont was mentioned more than Martindale was because of the existence of methadone concentrate.

In relation to Clause 10.1, Rosemont said that there had been no attempt to disguise the promotion of a prescription only medicine. The article simply gave factual information about the forms of methadone liquid that were available at the time of publication. There was

no advertising by Rosemont and the article could not be construed to be advertising on behalf of Rosemont.

Prescription only medicines could not be advertised to the general public. No advertisement of the products in question had been made and there could therefore be no breach of Clause 20.1. In relation to Clause 20.2, Rosemont said that the information presented was factual and balanced. There was no question of raising unfounded hopes of successful treatment or of misleading claims about safety (in fact there was a statement to the effect that concentrate methadone would not be dispensed widely by community services, because of a bigger risk of accidental overdose). There was no inducement for methadone users to seek alternative methadone products from their prescriber. The article pointed out that the newer concentrate would mainly be used by big prescribing clinics with supervised consumption programmes. This meant that there would be much less chance for illegal use of methadone.

The only question remaining was the question of "glamorising" the use of methadone. The aim of the publication, as presented to Rosemont when asked to be a sponsor, was to address the misconception amongst some practitioners and many clients that prevented opiate users presenting for, or complying with, methadone treatment. The tone adopted by the publication was to make it accessible and informative to the readers. In Rosemont's view it did not glamorise the use of methadone. Rosemont recognised that methadone "clients" by and large were unfortunate individuals who were prescribed methadone for opiate dependency. Rosemont considered that the sponsorship of "Juice" was a worthwhile way of giving something back in the form of factual information to this group of people. If it had wished to use the money for advertising purposes, it would have been used on conventional advertising in recognised professional publications.

In response to an enquiry from the Authority, Rosemont said that the publication was available for sale to the general public through the Institute for the Study of Drug Dependency, which distributed a number of publications in this field, although the specific group of the general public who would hear about and buy the publication were methadone users. Rosemont was not involved in the sale of the magazine but its representatives did give copies to professionals working in drug dependency units and clinics so that they were aware of the magazine's existence and could decide whether to use it as an information source for their clients. It was possible that some doctors might be given a copy and also some nurses and pharmacists working in the field of opioid dependency.

RULING

The Panel noted that the publication had the sub-title "the methadone magazine" and was devoted entirely to that substance, its properties and its use. The style, tone and content of the publication would not be to everyone's taste but it was not dissimilar to other publications in this particular field. The Panel considered that it was a specialised publication which was difficult to judge by the criteria which were usually applied to publications sponsored by the pharmaceutical industry. The Panel noted that the publication stated that it was not available on subscription but that issues would be produced as funding allowed, approximately every six months. The magazine's existence did not appear to be dependent upon Rosemont though, as stated in the publication, financial support from Rosemont enabled the publisher to keep the price down while retaining full editorial control. Rosemont was in a position of some conflict as it was a producer of methadone.

The Panel considered that the references to Rosemont's products were balanced in nature and not unacceptable. The Panel did not accept that the magazine constituted the advertising of prescription only medicines to the public and nor would it encourage patients to ask their doctors to prescribe a specific medicine. In view of the unusual nature of the publication, the Panel did not consider that it could be regarded as "glamorising" methadone.

The Panel did not consider that the Code had been breached and ruled accordingly.

Complaint received **23 August 1996**

Case completed **7 October 1996**

GP v SANDOZ

Disease area campaign to the public

A general practitioner complained about an advertisement in The Independent which was headed "There's no disguising problem toenails". The complainant accepted that the advertisement did not mention a product by name but advice was given by a freephone number to see a doctor to obtain a prescription for the problem.

The Panel noted that none of the materials relating to the campaign mentioned Sandoz's product, Lamisil, by either brand name or generic name. The materials did encourage patients to discuss treatments with their general practitioners and this might lead to patients asking their doctors for prescriptions. This was not necessarily unacceptable. There were a number of products other than Lamisil which were within the criteria referred to. The Panel was however concerned about the concept of this type of advertisement appearing in the national press. In this particular instance, however, the Panel considered that the materials were reasonable and no breach of the Code was ruled.

A general practitioner, complained about an advertisement in The Independent, 22 August 1996. The advertisement was headed "There's no disguising problem toenails". The advertisement said that thick, brittle, discoloured toenails might be caused by a fungal infection. A free leaflet and advice was offered and a freephone telephone number was given. The advertisement referred to the Stepwise campaign and said that it was sponsored by Sandoz.

COMPLAINT

The complainant said that although the advertisement did not mention any product by name, advice was given via a freephone number to see a doctor to obtain a prescription for the problem. To the complainant's knowledge, there was no over the counter preparation available for the condition at present. A breach of Clause 20.1 of the Code was alleged.

The Authority noted that a similar complaint had been received (Case AUTH/313/6/95) in which the Code of Practice Panel had ruled no breach of the Code. Paragraph 5.1 of the Constitution and Procedure stated that the Director of the Authority should normally allow a complaint to proceed if it covered matters similar to those in a decision of the Code of Practice Panel which had not been subject of an appeal to the Code of Practice Appeal Board. As no appeal had been made in the previous case this new complaint was allowed to proceed.

RESPONSE

Sandoz advised that the current Stepwise programme, of which the advertisement in The Independent was a part, utilised the same materials as those previously reviewed by the Authority in relation to Case AUTH/313/6/95 with the addition of a follow up patient information booklet "Know your nails Identifying nail problems" (ref step 5). This additional booklet was forwarded to patients who had contacted Stepwise and had received the original "Feet and nails Stamping out problems" booklet (ref step 1) and had chosen to stay on the mailing list to receive additional information when it became available. The additional booklet "Know your nails Identifying nail problems" examined a range of common nail problems and provided advice to patients on how to manage them, as well as providing useful tips on how to keep the nails healthy.

The company referred to previous correspondence on this matter. The aim of the Stepwise programme was to provide helpful information to the public about foot and nail care generally as well as alerting people who suffered from some of the common foot and nail problems that they could be fungal in nature and thus infectious. The programme materials had been devised to encourage patients to take more interest in their own healthcare. Copies of the materials were provided. These were a leaflet "Stamping out athlete's foot" (ref step 2), a leaflet "How to recognise problem toenails when you see them" (ref step 3) and the two booklets referred to above "Feet and nails Stamping out problems" and "Know your nails Identifying nail problems". The company submitted that the materials contained therapeutic area information and advice only and no reference to any prescription medicine.

The programme was based on research indicating that there was a large untreated reservoir of patients in the community who did not recognise they had a fungal infection or who had received ineffective therapy in the past which had led them to believe that their condition was untreatable. In the case of athletes foot, which was thought to affect 10 to 15% of the UK population, the problem was often lack of adequate advice on duration of treatment and good foot hygiene in a population of patients, only a quarter of whom would have discussed their condition with their doctor. If untreated, athletes foot and onychomycosis served as reservoirs of infection which could spread to other parts of the patient's body, their family and into the environment, especially among users of communal bathing places. It had been postulated that, without an effective public health campaign, this level of ignorance would lead to an increased presence of dermatophyte infection.

Sandoz was aware that the provision of educational material to patients had been the subject of considerable controversy. In view of this the company had carried out a thorough review of the regulatory framework and Code of Practice precedents on provision of information to patients and developed some clear guidelines for compliance before fully developing the Stepwise programme. A copy of the analysis was provided.

RULING

The Panel noted that the materials provided by Sandoz were the same as those at issue in Case AUTH/313/6/95 with the addition of the booklet "Know your nails

Identifying nail problems".

The Panel noted that none of the materials referred to products. The booklet "Know your nails Identifying nail problems" gave information about a number of nail problems such as white spots, ingrowing toenails etc. In relation to fungal nail infections, the booklet stated that "If you think you have the condition you should visit your family doctor, who can now prescribe effective treatment. If you have tried treatments for this condition in the past with little success you may find it is now worth going back to your doctor for further advice". The other materials contained generally similar statements about the treatment of fungal nail infections. Some of the materials mentioned that treatments taken by mouth for fungal nail infections would also cure athletes foot.

The Panel noted that none of these materials mentioned Sandoz's product Lamisil by either brand name or generic name. The materials did encourage patients to discuss treatments with their general practitioners and this might lead to patients asking their doctors for prescriptions. This was not necessarily unacceptable. There were a number of products other than Lamisil that were within the criteria referred to, ie prescribable oral treatment for fungal nail infections and athletes foot. It was up to the doctor to decide which product to prescribe if any.

The Panel decided that on balance the materials were reasonable in relation to the requirements of Clauses 20.1 and 20.2 of the Code.

Turning to the advertisement in The Independent, the Panel noted there was no product name given in it. The Panel accepted that the advertisement would encourage patients to ask for information about problem toenails. The advertisement offered a free leaflet and advice to callers. The patients that went to see their doctors about their problem toenails would not be able to ask for a particular product by name. The doctor would have to decide whether or not to prescribe a product. The Panel decided that it was not an advertisement to the public for a prescription only medicine.

The Panel was, however, concerned about the concept of this type of advertisement appearing in the national press. In addition to the content of such an advertisement, an important factor in determining its acceptability would be the nature of the materials provided to enquirers. In this particular instance, the Panel considered the materials to be reasonable. The Panel ruled no breach of Clause 20.1.

Complaint received **27 August 1996**

Case completed **2 October 1996**

CASE AUTH/460/9/96

SERONO v BRITANNIA

Promotion of Alec

Serono complained about a number of promotional items for Alec issued by Britannia.

A review of clinical papers was ruled to be in breach of the Code as it did not include prescribing information for Alec. Prescribing information on two other items was ruled to be acceptable as the name of the medicine had not been omitted as alleged.

There were no reference numbers printed on any of the promotional items but this was not a requirement of the Code. The Panel noted that Britannia attached the certificate to the actual piece as a means of identifying what had been certified.

Teddy bears bearing the brand name Alec were ruled not to be in breach of the Code but the Panel had misgivings about their distribution at exhibitions and advised that the distribution of such toys should be targeted directly to surgeries or consulting rooms.

Serono Laboratories (UK) Ltd complained about the promotion of Alec by Britannia Pharmaceuticals Limited. There were a number of allegations which were considered as follows.

1 Document entitled "Alec & Respiratory Distress Syndrome Review of main clinical papers"

This was a four page A4 document. The front page had the product name in logo type together with the product marque, a hot air balloon which bore the product name. The hot air balloon also appeared on some of the inside pages. The document gave background information on respiratory distress syndrome, a synopsis of two clinical trials with Alec and a review of the costs of surfactant treatment. The last page was headed "Alec - Main features" underneath which were eight stab points.

COMPLAINT

Serono alleged that this piece did not include prescribing information for Alec in breach of Clause 4.2 of the Code.

RESPONSE

Britannia accepted the complaint. The piece had originally been drawn up as an internal document and was inadvertently printed as a promotional piece without going through the internal approval procedures. This had prompted a review of Britannia's internal procedure to ensure that such an error was not repeated.

All copies of this piece of literature were to be withdrawn from Britannia's promotional activities.

RULING

The Panel considered that although the document was a review of clinical papers it had been presented in a promotional style. The front cover featured the product name prominently in logo type together with the product

marque. In the review of the two clinical trials the product name, Alec, only ever appeared in capital letters. In addition the document also compared the cost of Alec with the cost of other available surfactants and listed eight "main features" of Alec on the back page. The Panel regarded the document as promotional and considered that it should have included prescribing information for Alec. The Panel therefore ruled a breach of Clause 4.1.

2 A folder entitled "Alec, A Pure and Simple Solution"

This was a folder to hold A4 documents. It had a visual of the hot air balloon on the front cover and prescribing information was printed on the inside front cover beneath a pack shot. The inside flap carried the name of the company together with the product marque and name in logo type. In addition to the company name and address and the product name in logo type, the back of the folder carried some claims for Alec.

COMPLAINT

Serono alleged that this piece was in breach of Clause 4.2 of the Code. It included a section headed "Abridged Prescribing Information". If this was meant to be in substitution for prescribing information, it did not include the name of the medicine and nor did it contain the inverted black triangle symbol. In addition, the black triangle on the front cover was less than the required size.

RESPONSE

Britannia submitted that the requirement that the product name was given in the prescribing information was fulfilled. The brand name Alec appeared 14 times and the generic name, pumactant, appeared 4 times. Immediately above the prescribing information there was a pack shot of the product with the name Alec clearly visible. Britannia could not accept that the name of the product was not clearly stated.

In addition Britannia submitted that the use of the black triangle was not a requirement of the Code. However, in response to the point raised by Serono, Britannia pointed out that the inverted black triangle appeared in the correct size in the most prominent position on the back cover.

RULING

The Panel noted that Clause 4.1 of the Code required that prescribing information be provided in all promotional material, except for abbreviated advertisements (Clause 5) and promotional aids which met the requirements of Clause 18.3. Prescribing information had to be a succinct summary of the data sheet or summary of product characteristics and Clause 4.2 set out what must be included. It was not possible to breach Clause 4.2, omission of information would be a breach of Clause 4.1 of the Code.

The Panel noted that the document folder was a promotional item. The folder included the product name in logo type, the product marque and claims for Alec and so required prescribing information. The inside front cover contained a section of text headed "Abridged Prescribing Information". The information given under the heading was that set out in Clause 4.2 of the Code. The Panel considered that the heading "Abridged Prescribing Information" was acceptable. The Code did not require the term "Prescribing Information" to be used exclusively. The Panel noted that the text included the generic name and the brand name and so fulfilled the first requirement of Clause 4.2 of the Code. In addition, above the heading, there was a pack shot of the medicine such that the brand name, Alec, together with the adjacent generic name, were clearly visible. The Panel ruled no breach of Clause 4.1 of the Code.

The Panel noted that the supplementary information to Clause 4.2 of the Code gave advice regarding the size and positioning of the inverted black triangle although its use was not a Code of Practice requirement. The symbol should normally not measure less than 5mm per side although a smaller size, 3mm per side was allowable on A5 material and a larger size of 7.5mm per side should be included on A3 material. The symbol should appear once, next to the most prominent display of the product name.

The Panel noted that the folder was larger than A4 and so required a triangle of 7.5mm per side and this should be next to the most prominent display of the product name. The Panel considered that the most prominent display of the product name was on the front cover of the folder as part of the product marque. There was a black triangle next to this mention of the product name but it was less than 5mm per side. The Panel noted that while the back cover of the folder had a black triangle next to the product name, this was not the most prominent display of the product name. The Panel considered that Britannia would be well advised to increase the size of the triangle on the front cover of the folder so that each side was 7.5mm.

3 Alec Administration Guide

This was a twelve page booklet giving a step by step guide to the reconstitution, preparation and administration of Alec. The hot air balloon appeared on the front cover and prescribing information was given on the inside back page. The back cover of the booklet gave the same details as given on the back of the folder at issue in Point 2 above.

COMPLAINT

Serono alleged that this piece was in breach of Clause 4.2 of the Code. The piece had incomplete prescribing information which lacked both the product name and the inverted black triangle symbol.

RESPONSE

Britannia submitted that the requirement that the product name was given in the prescribing information was fulfilled. The brand name Alec appeared 14 times and the generic name pumactant appeared 4 times.

As before, the use of the black triangle was not a requirement of the Code. However, in response to the point raised by Serono, Britannia pointed out that the inverted black triangle appeared in the correct size in the most prominent position on the back cover. The front cover was a graphic of a balloon with the name Alec on the balloon. The title Alec together with key product

features appeared on the back cover.

RULING

The Panel considered that its ruling in Point 2 above similarly applied to this Point.

The "Abridged Prescribing Information" contained all the elements required by Clause 4.2 of the Code including the product name. In addition, the product marque next to the abridged prescribing information clearly showed the brand name with the generic name adjacent to it. No breach of the Code was ruled.

The Administration Guide was smaller than A4 but larger than A5 and so the Panel considered that the black triangle symbol on this piece should have sides of 5mm. A black triangle did appear next to the product name on the back cover but this was not the most prominent display of the brand name. The Panel considered that the 5mm black triangle should appear on the front cover.

4 Reference numbers

COMPLAINT

Serono complained that there were no reference numbers on the promotional material to record certification of the material.

RESPONSE

Britannia submitted that there was no requirement for reference numbers to appear on each piece of promotional literature. The company's internal procedure required that each piece was given a unique reference number and a copy of the actual piece was attached to the final signed approval form.

However, in light of the error that occurred, and which was discussed in Point 1, this procedure was being reviewed.

RULING

The Panel noted that Clause 14 required that promotional material must not be issued unless its final form had been certified. Guidelines printed in the Code of Practice booklet contained advice on certification of promotional material. The guidelines did not, however, form part of the Code. They merely set out guidance on what represented good practice. There was no requirement under the Code for a reference number to appear on the final item. The Panel therefore ruled no breach of the Code. The Panel noted Britannia's practice of attaching the final signed approval form to a copy of the actual piece as a way of identifying what had actually been certified.

5 Teddy bears

COMPLAINT

Serono believed that Britannia were giving away teddy bears at exhibitions and meetings and alleged that these contravened Clause 18.2 of the Code. Teddy bears had no medical use and nor were they of use to the patient as the product in question was used to treat neonates.

RESPONSE

Britannia submitted that the teddy bears did have a use in medical practice - to amuse small children in a consulting room, and were also of use to the patient, in as much as a teddy bear was a reasonable thing to give a new born baby as a means of stimulation and amusement.

The teddy bears were purchased at a cost of £3.29 each and were, therefore, within the guidelines of an inexpensive gift, i.e. one that cost no more than £5.00 excluding VAT.

RULING

The Panel noted that the supplementary information to Clause 18.2 allowed companies to provide doctors with toys so that young children could be amused and distracted during visits to the surgery. Such gifts must be inexpensive, i.e. cost the donor company no more than £5.00 excluding VAT. The teddy bears in question cost £3.29. The Panel considered that the teddy bear was a suitable item for a young child to play with during a visit to the doctor. It was not unacceptable to give the teddy bear in question to a child in hospital. The Panel therefore ruled no breach of Clause 18.2 of the Code. The fact that the product involved was for neonates did not mean that the gift was unacceptable.

Notwithstanding the above ruling, the Panel had misgivings about the mode of distribution of the teddy bears. The Panel considered that, by giving them out at exhibitions and meetings, the teddy bears might well not be loaned to, or given to, patients. It was possible that they would be taken for personal use. Companies would be well advised to target the distribution of toys direct to surgeries and consulting rooms and recipients should be told that the gift was for use by children visiting the doctor or children in hospital.

Complaint received **5 September 1996**

Case completed **23 October 1996**

CASE AUTH/461/9/96

YAMANOUCHI v BIOGLAN

Promotion of Benzamycin

Yamanouchi complained about a journal advertisement and a mailing on Benzamycin issued by Bioglan. There were six allegations.

The Panel ruled that the advertisement resembled editorial matter in breach of the Code. The Panel also ruled that a diagram was misleading in that it had not been made clear that the diagram in the advertisement had been modified from that in the quoted reference. No breach of the Code was ruled in relation to a reference to 72 patients being involved in a study whereas only 67 patients completed the actual study. The Panel ruled no breach of the Code with regard to an allegation that data from a study implied that 67% of patients found Benzamycin acceptable. No breach of the Code was ruled in relation to the mention of a health professional's name in the advertisement. Finally, no breach of the Code was ruled in relation to the omission of a bar from a bar chart, given that in these particular circumstances the layout was such that readers would not be misled.

Yamanouchi Pharma Limited complained about the promotion of Benzamycin by Bioglan Laboratories Limited. Bioglan, although not a member of the ABPI, had nevertheless agreed to comply with the Code.

The material at issue was a page headed "Advertisement Feature" which appeared in Pulse, 10 August 1996. The advertisement consisted of sections headed "Benzamycin efficacy and speed of action", "Rising to the challenge of antibiotic resistance" and "Nurses help GPs to review acne care". Prescribing information was also included on the page together with an illustration and claim for Benzamycin in the style of a typical abbreviated advertisement. There was also an allegation about a mailing (leaflet ref 191 00 104).

The allegations were considered as follows.

1 Disguised promotion

COMPLAINT

Yamanouchi alleged that the promotional material was difficult to identify as an advertisement, particularly as it was juxtaposed to a feature on dermatology photographs. The company alleged that the advertisement was disguised promotion as it strongly resembled editorial material. A breach of Clause 10.1 of the Code was alleged.

RESPONSE

Bioglan said that the material was clearly identified by the heading "Advertisement Feature". It was also printed in a different font with double spacing to differentiate it from the Pulse house style and avoid confusion with editorial material. The feature on the opposite page was beyond Bioglan's control.

RULING

The Panel noted that the supplementary information to Clause 10.1 of the Code stated that advertisements in journals must not resemble editorial matter. The Panel considered that, as a matter of principle, material did not have to be exactly the same as the actual editorial material in a particular journal in order for it to be said to resemble editorial matter. It would, however, have to have the general appearance of editorial material. Secondly, the Panel considered that the fact that material said that it was an advertisement did not necessarily mean that it was not disguised promotion. That would depend on the nature and prominence of such a statement.

The Panel examined the page in question and noted that it was headed "Advertisement Feature". The layout of the three articles was not exactly the same as the editorial material in Pulse in that double lined spacing and a different font had been used. The Panel noted that the page included a blue line under the main heading and a diagram appeared on a blue background. The shade of blue chosen was similar to the shade of blue used in the editorial text. The Panel considered that overall the company had not made sufficient effort to distinguish the advertisement from the editorial material. In the Panel's view the advertisement resembled editorial material. The Panel therefore ruled a breach of Clause 10.1 of the Code.

2 Number of patients in a study

COMPLAINT

Yamanouchi pointed out that the article "Benzamycin efficacy and speed of action" referred to 72 patients being involved in a study. However, from the actual study report, it could be seen that only 67 patients had completed the study.

RESPONSE

Bioglan accepted that Yamanouchi was correct in that the advertisement contained the phrase "10 week study involving 72 patients with mild to moderate acne...". The study in question was a clinical trial by Dr A Chu *et al.*

In correspondence with Yamanouchi, Bioglan had disputed Yamanouchi's claim of inaccuracy, but, in the interests of goodwill, had agreed that it would not refer to the number of patients entering the trial and instead refer to the number completing the trial to avoid any possible confusion.

RULING

The Panel noted that 72 patients had been entered into a parallel group study designed to determine the comparative efficacy and safety of Benzamycin and erythromycin/zinc solution. Three patients had discontinued the study due to adverse events. It was not easy to ascertain what had happened to the other two patients. The Panel considered that it would be helpful to

readers in such circumstances to give the starting number of patients, the finishing number of patients and the reasons for drop out. The Panel noted that the data from the study which appeared later in the article had been calculated using the number of patients completing the study.

The Panel decided that it was true to say that the study involved 72 patients but considered that it would have been helpful to have given the number finishing the study. Given the fact that the number of drop outs was relatively small and that the results appeared to be calculated on the number of patients completing the study, the Panel did not consider that readers would be misled. No breach of Clause 7.2 was ruled.

3 Confusion of Data

COMPLAINT

Yamanouchi referred to the final paragraph in the article headed "Benzamycin efficacy and speed of action". The final paragraph discussed acceptability but then went on to quote figures for patients' global assessments for efficacy. Bioglan claimed that 67% of Benzamycin treated patients' and 28% of erythromycin zinc treated patients reported 75% improvement. These figures, as the patient global evaluation, differed from the figures presented in the preceding paragraph for physician global evaluation, causing some degree of confusion. The figures for cosmetic acceptability were not given but tended towards statistical significance in favour of Benzamycin $p = 0.073$. Yamanouchi alleged that this appeared to be a confusing array of data, ending with the implication that 67% of patients found Benzamycin acceptable. This was misleading in breach of Clause 7.3 of the Code.

RESPONSE

Bioglan accepted that Yamanouchi had quoted the final paragraph accurately. In the preceding and separate paragraph the material stated that "52% of Benzamycin patients were judged to have shown a 75% or better global improvement compared to 10% of erythromycin zinc patients". This was again a clear and accurate statement.

Bioglan submitted that the figures for physician and for patient evaluation of global improvement were clearly and separately stated. The fact that patients also evaluated the acceptability of the two treatments was also mentioned, but in the interests of brevity and clarity these results were not included even though they favoured Benzamycin.

RULING

The Panel examined the results section of the article and considered that it was clear which results were the investigators' results and views and which were the results from the patient evaluations. It was not surprising that these differed. The Panel did not accept that the data was misleading. It had been presented in separate paragraphs and would be clear to readers.

The Panel considered that the use of the term "acceptability" in the statement "Patients in the study evaluated the acceptability of the two treatments ..." was somewhat confusing given that the word was used in relation to patients' global evaluations which, according to the study, were based on overall improvement in the patients' condition since initiating therapy. The Panel did not consider that the reference to acceptability would be taken as meaning cosmetic acceptability. In the Panel's view it would have been helpful if the data had been explained better in this regard but it was not misleading.

The Panel ruled no breach of the Code.

4 Protocol developed by a dermatologist

COMPLAINT

Yamanouchi said that an article in the advertisement "Nurses help GPs to review acne care" stated that the protocol developed by Professor Cunliffe recommended the use of topical therapies such as erythromycin and benzoyl peroxide as first line treatment of mild to moderate acne to minimise the risk of antibiotic resistance and improve patient compliance. The actual reference did not support this statement. The reference discussed different therapies and a diagram implied that benzoyl peroxide, topical antibiotics and azelaic acid could be used as first line treatment for mild inflammatory acne. The diagram provided in the advertisement did not agree with the diagram in the reference. Yamanouchi alleged that this was misleading in breach of Clause 7.2.

RESPONSE

Bioglan submitted that the reference, an article in Prescriber, and accompanying management protocol flow diagram clearly showed that benzoyl peroxide, topical antibiotics and azelaic acid were the recommended first line treatments for mild to moderate inflammatory acne. The text also discussed the importance of erythromycin in combination with either zinc or benzoyl peroxide in minimising resistance. In short, the reference supported the statements in the advertisement.

The diagram in the advertisement was a fuller version of the diagram in the reference in that combination therapies and vitamin A derivatives had been added. These additions were made by Dr Chu to update and extend the protocol as published in 'Skin Care in Practice'. The company accepted that with hindsight it should have referenced the diagram in the advertisement to the 'Skin Care in Practice' article. However, the additions made in no way strengthened the Benzamycin positioning, indeed quite the opposite, it gave a fuller picture of the accepted first line treatment of mild acne.

RULING

The Panel examined the advertisement which stated "Following a management protocol such as one developed by Professor Bill Cunliffe, can help to assess acne grade..." It then went on to say that "The protocol advises the use of topical combination therapy such as erythromycin and benzoyl peroxide as the first line approach in treating mild to moderate acne..." Immediately below there was a diagram headed "Management protocol for acne based on severity".

The Panel considered that the implication of the advertisement was that the management protocol shown in the diagram was Professor Bill Cunliffe's protocol and this was not so. Professor Cunliffe's protocol as printed in Prescriber did not refer to combination therapies or vitamin A derivatives. It should have been made clear in the material that the protocol had been modified. The Panel considered that the use of the diagram was misleading and ruled a breach of Clause 7.2 of the Code.

5 Use of a professor's name in advertising

COMPLAINT

Yamanouchi alleged that the use of Professor Bill Cunliffe's name in the advertisement implied that he supported the advertisement. The company was unaware if this was the case or if he was aware that his name was being used in an advertisement. The company alleged that this brought the industry into disrepute.

RESPONSE

Bioglan said that Professor Cunliffe's name was referred to and correctly referenced to a recently published article which he wrote. As such, it was a statement of fact that he prepared a protocol and that in the article he advocated the use of products such as combination topicals in treating mild to moderate acne. Any implication of the Professor's support of the advertisement was subjective and not intended by Bioglan.

RULING

The Panel noted that the only mention of Professor Cunliffe by name was in the text of the article and in the list of references at the bottom of the advertisement. The Panel did not consider that this was unreasonable. Professor Cunliffe's name had been used in association with the management of acne generally. There was no implication that Professor Cunliffe endorsed any product. The Panel ruled no breach of the Code.

6 Omission of a bar in a leaflet

This allegation concerned a mailing sent by Bioglan. The mailing included a bar chart showing results obtained from a study comparing Benzamycin gel and erythromycin/zinc. The results were given in the form of a bar and the value of each bar was confirmed by a number printed at the end of each bar.

COMPLAINT

Yamanouchi alleged that the bar chart omitted the erythromycin/zinc bar at 4 weeks. This was a gross misrepresentation of the data in breach of Clauses 7.2 and 7.6. The company also alleged that this was not maintaining high standards of promotion in breach of Clause 9.1 and brought into question the copy approval process at Bioglan.

RESPONSE

Bioglan accepted that there was an omission on the mailing which resulted from a printing error. This was only picked up after the item had been mailed. The same data source had been used correctly in other materials. Following this problem Benzamycin was no longer handled by the agency responsible and the procedures within suppliers were closely monitored by the marketing group. Bioglan submitted that its procedures were in line with maintaining the appropriate level of accuracy and standards required of a pharmaceutical company.

RULING

The Panel noted that the bar chart omitted the actual bar but it had included the figure, 44, in the place where it would have been expected. The Panel noted that the fact that a printer had made an error was irrelevant, the company was responsible for the material that went out.

The Panel examined the material and considered that, in the circumstances, readers would not be misled. The percentage figures given after 4 weeks therapy were 69 for Benzamycin gel and a figure of 44. Readers would realise that the 44 related to erythromycin/zinc. The Panel considered that the material should have included the bar but, given the circumstances and the layout of the chart, readers would not be misled. The Panel therefore ruled no breach of the Code.

Complaint received **10 September 1996**

Case completed **16 October 1996**

CASE AUTH/462/9/96

PHARMACIST v BIOGLAN

Cocois journal advertisement

A pharmacist complained about a journal advertisement for Cocois scalp ointment issued by Bioglan. The complainant alleged that the claim "When pharmacy treatments won't wash" was disparaging of the pharmacy profession, implied that the product was superior to other non-prescription medicines and was outside the licensed indication which was as an adjunctive therapy.

The Panel ruled that the claim was misleading as it gave the impression that Cocois was not a pharmacy treatment and this was not so. Cocois, as a GSL product, was available for pharmacists to recommend and supply. The Panel ruled no breach of the Code regarding the other allegations.

The complaint concerned a Cocois scalp ointment advertisement issued by Bioglan which appeared in Doctor, 29 August 1996. The advertisement was headed "Scaly Scalp? When pharmacy treatments won't wash". Bioglan was not a member of the ABPI but had nevertheless agreed to comply with the Code.

COMPLAINT

A pharmacist alleged that the claim "When pharmacy treatments won't wash" was disparaging of the profession of pharmacy and any products that a pharmacist might recommend or supply. The complainant considered that as the product was a general sales list (GSL) medicine that could be purchased from a petrol station or grocer, the claim was a bit rich. Bioglan might not be prepared to sell its product to Tesco or Esso, but that would not preclude those companies obtaining it from a secondary supplier.

The complainant also alleged that the claim suggested that the product was superior to other licensed products which were not prescription medicines. This claim was not in keeping with the product's data sheet or product licence which said that it was an adjunctive treatment.

RESPONSE

Bioglan said that Cocois was a coal tar ointment used in the treatment of scaly scalp diseases such as psoriasis, eczema, seborrhoeic dermatitis and dandruff. Scaly scalp, especially in psoriasis and eczema, was a chronic relapsing condition for which there was no cure. All treatments were attempts to control the problem and might therefore fall short of patients' expectations. As a result it was not unusual for patients to ask their doctor for further help having already tried one or more medications purchased over the counter. The message to doctors in the advertisement was to think about prescribing Cocois to these patients.

The reasoning behind the advice was twofold. Firstly, Cocois was not actively promoted through pharmacies as an OTC and it was therefore unlikely that patients would have already tried it. Secondly, OTC treatments for scaly scalps were commonly coal tar shampoos and, in a clinical trial by Monk et al 1995, Cocois had been shown to be significantly superior to coal tar shampoo at removing scale.

With regard to the allegation that the claim was disparaging to the profession of pharmacy, the company submitted that the objection was difficult to understand as the advertisement contained no reference, direct or indirect, to the profession of pharmacy. The claim expressed the view that some patients sought help from their doctors after trying to solve their problems with OTC medication. Was the complainant suggesting that this was not true? Presumably not as any practising pharmacist or doctor knew that it was. Or was the concern that it was true but should not be mentioned because it somehow implied criticism of the pharmacist who supplied the OTC medication. The company submitted that this was an unreasonable and extreme view. With regard to the allegation that the claim was disparaging to any products that a pharmacy might recommend or supply, the company accepted that the objection had some relevance as the claim did refer to pharmacy treatments. However it was self evident that the claim was not disparaging to anybody or anything. By definition it did not "speak contemptuously, belittle or damage the reputation".

Finally with regard to the allegation that the claim suggested that Cocois was superior to other licensed products other than prescription medicines and that this was not in keeping with the product's data sheet or the licence which said that it was an adjunctive treatment, the company submitted there were clinical data to show that Cocois was superior to coal tar shampoos in removing scale. The company was confused by the logic which suggested that a claim of superiority was not in keeping with an adjunctive treatment.

RULING

The Panel noted that Cocois scalp ointment was a GSL product. It could therefore be sold by supermarkets etc as well as by pharmacies. The Panel did not accept the submission that as Cocois was not actually promoted through pharmacies as an OTC medicine, it was unlikely that patients would have tried it. It was quite possible that pharmacists would recommend Cocois to patients irrespective of whether it had been specifically promoted to them.

The Panel noted that the advertisement was addressed to doctors. The claim "When pharmacy treatments won't wash" would be likely to be interpreted by the audience as meaning that when products available from the pharmacies did not work for the condition, then the prescriber should try Cocois.

The Panel considered that the claim was misleading as it gave the impression that Cocois was not a pharmacy treatment and this was not so. Cocois, as a GSL product, was available for pharmacists to recommend and supply.

The Panel therefore ruled a breach of Clause 7.2 of the Code.

The Panel did not accept that the advertisement was disparaging of pharmacists or products that a pharmacist might recommend or supply. Nor did the Panel accept that the advertisement was claiming superiority for Cocois over other treatments and that this was not in keeping with its use as an adjunctive treatment. No breach of the Code was ruled in this regard.

Complaint received 6 September 1996

Case completed 10 October 1996

CASE AUTH/464/9/96

DIRECTOR/PARAGRAPH 16 v LEO

Dovonex competition

A competition noted by the Panel in its consideration of an earlier case was taken up with Leo under Paragraph 16 of the Constitution and Procedure. The competition was one in which entrants had to mark a bar chart to show where they judged the relative efficacy of tacalcitol to be compared to that given for Dovonex.

The Panel accepted that the competition had a scientific basis but considered that the question posed was so difficult that entrants could do no more than guess the answer. The substantial prizes on offer were unacceptable given that the competition was judged not to be a *bona fide* test of skill and a breach of the Code was ruled.

COMPLAINT

The complaint arose from the Panel's consideration of Case AUTH/453/8/96 which concerned a conference poster used by Leo Pharmaceuticals Limited to draw attention to a competition. The Panel considered that there was a possible breach of Clause 18 of the Code in relation to the competition and decided that the matter should be taken up with Leo under the provisions of Paragraph 16 of the Constitution and Procedure.

The basis of the competition was that conference delegates were invited to judge the efficacy of tacalcitol (E Merck Pharmaceuticals' product, Curatoderm) compared to that of Dovonex (Leo's product). The entry form for the competition featured a vertical bar chart which showed Dovonex with an efficacy of 73.2%. Instead of a bar for tacalcitol there was a dotted line. Delegates were asked to mark a cross on this line to show where they judged the efficacy of tacalcitol to be.

The Panel considered that the question asked was a difficult one requiring expert knowledge and queried whether the competition was a test of skill or a matter of guesswork. Both the cost and relevance of the prize, which was an electronic personal organiser, were questioned.

Leo's attention was drawn to the requirements of Clauses 18.2 and 9.1 of the Code.

RESPONSE

Leo drew attention to the fact that this competition was held at a meeting of the British Association of Dermatologists. The predominant attendees were consultant dermatologists. As such, the participants would be expected to have considerable knowledge of the scientific background upon which this competition was based. This competition was directed to dermatologists and required a significant level of scientific knowledge and clinical expertise.

The scientific background was as follows:

1. There were data in the literature in respect of at least four different vitamin D analogues, in various stages of development, for the treatment of psoriasis and other proliferative or inflammatory diseases. These included calcipotriol, tacalcitol, calcitriol and 22 oxa calcitriol.

2. The therapeutic action of these analogues was in part a common property of all vitamin D analogues and in part molecule specific. That was to say they shared general common features but there were differences which were molecule specific. To judge relative efficacy in psoriasis required a degree of scientific skill.

3. It was further very important to realise that, for any given molecule, details of the formulation might have a very dramatic effect. In Leo's own calcipotriol development programme, for example, there were very clear clinical differences of some magnitude between ointment, cream, gel and solution both in terms of efficacy and side effects. To judge relative efficacy of different formulations (ie calcipotriol in the Leo ointment base and tacalcitol in the E Merck ointment base) required a degree of expert knowledge.

4. The dose/response relationship was a significant factor in considering relative efficacy. The clinician would need to assess the likely relative efficacy of tacalcitol at a concentration of 4mg with calcipotriol at a concentration of 50 mg.

5. A further variable which needed to be taken into account in answering this competition was the frequency of application, ie Dovonex was given twice daily and tacalcitol given once daily. Further information was made available to any competitor, on request, in respect of Dovonex once daily compared with Dovonex twice daily and in respect of Dovonex once daily vs tacalcitol once daily.

A considerable amount of clinical experience and scientific ability was required in order to judge the

relative importance of the variables discussed above in order to reach a conclusion in respect of the relative efficacy of these two vitamin D analogue formulations.

Leo submitted that the cost of the personal organiser was less than £100. This was a serious competition; the prizes were few in number, ie one only on each of two days, and the value was not out of proportion to the skill required in this competition. Indeed, the Panel had already pointed out that the depth of knowledge required to complete this competition was considerable.

A personal organiser was relevant to the work of any professional individual who was required within his/her working environment and practice, to record, in a portable fashion, complex information which was essential to carry out daily duties in an efficient and timely manner.

With regard to the requirements of Clause 9.1 of the Code, Leo submitted that the materials used recognised the special nature of medicines and the professional standing of the audience. Leo could not see that this competition could in any way cause offence to the participants. The Panel had itself accepted that the question raised was difficult and, Leo suggested, maintained a high scientific standard. The materials used in this competition were in good taste and not likely to cause offence.

RULING

The Panel did not accept that just because a competition was difficult it was necessarily a test of skill. In the Panel's opinion, questions could be made so difficult that, even if a person was aware of all the factors involved, he or she would still only be able to make an educated guess as to the right answer. The Panel accepted that there was a scientific basis for the competition in question and that entrants would be able to appreciate the factors involved. The Panel considered, however, that the nature of the question asked effectively reduced the task to one of conjecture. It was clearly possible, but highly unlikely, that dermatologists would know the correct answer or be able to derive it solely from the data supplied by Leo.

The Panel considered that the nature of the competition meant that entrants would inevitably have to guess the answer. This impression was reinforced by Leo's representatives' briefing document referring to the "tacalcitol quiz" which stated that delegates would be invited "to guess the level of tacalcitol activity".

The Panel accepted that the prizes offered in the competition, electronic personal organisers, were relevant to the potential recipients' work. The prizes were within the maximum acceptable cost of £100 plus VAT and were limited in number. The Panel noted, however, that the supplementary information to Clause 18.2 of the Code stated that prizes of a higher value than would ordinarily be acceptable for promotional aids were only acceptable where the competition itself was an acceptable one and the prizes offered were not out of proportion to the skill required in the competition.

The Panel considered that the competition was unacceptable as it was not a *bona fide* test of skill given that entrants could do no more than guess the answer. As a result prizes costing more than that allowed for a promotional aid (£5 excluding VAT) were not allowed. The Panel ruled a breach of Clause 18.1 of the Code.

Proceedings commenced **11 September 1996**

Case completed **21 October 1996**

CODE OF PRACTICE REVIEW - NOVEMBER 1996

Cases in which a breach of the Code was ruled are indexed in **bold** type.

400/2/96	**Leo v E Merck**	**Curatoderm journal advertisement**	**Breach 7.2**	**Appeals by both complainant & respondent**
416/3/96	**Lundbeck v Lilly**	**Prozac leavepiece**	**Breach 7.2**	**Appeal by respondent**
421/4/96	**Director/Scrutiny v Norton Healthcare**	**Inducements to purchase**	**Breach 18.1**	**Appeal by respondent**
434/5/96	GP v Glaxo Wellcome	"Dear Doctor" letters on Imigran-50	No breach	No appeal
435/5/96	**Schwarz Pharma v Boehringer Ingelheim**	**Motens detail aid**	**Breach 7.2**	**No appeal**
436/6/96	Solvay v E Merck	Promotion of FemSeven	No breach	No appeal
437/6/96	Hospital Pharmacist v SmithKline Beecham	Unsolicited supply of Famvir	No breach	No appeal
439/6/96	**Director v Janssen-Cilag**	**Breach of undertaking**	**Breach 2 & 21**	**Appeal by respondent**
440/6/96	Leo v E Merck	Curatoderm journal advertisement	No breach	Appeal by complainant
441/6/96	**Seton v Houghs**	**Triclosan Information document**	**Breach 3.1,3.2 & 4.1**	**No appeal**
442/7/96	**Janssen-Cilag v Parke Davis**	**Journal advertisement relating to previous Code of Practice ruling**	**Breach 2, 4.1, 8.1 & 9.1**	**Appeals by both complainant & respondent**
443/7/96	**Ciba v Glaxo Wellcome**	**Serevent leavepiece**	**Breach 7.2**	**No appeal**
444/7/96	**Janssen-Cilag v Parke Davis**	**Letter relating to previous Code of Practice rulings**	**Breach 2, 4.1, 8.1 & 9.1**	**Appeal by respondent**
445/7/96	Consultant Physician v Lederle	Gastro Care Programme	No breach	No appeal
447/7/96	GP v Sandoz	Climesse journal advertisement	No breach	No appeal
450/8/96	**Pfizer v Boehringer Ingelheim**	**Motens detail aid**	**Breach 7.2**	**No appeal**
451/8/96	**SmithKline Beecham v Pasteur Merieux MSD**	**Avaxim journal advertisements**	**Breach 7.2 & 7.7**	**No appeal**
453/8/96	**E Merck v Leo**	**Dovonex poster**	**Breach 8.1**	**No appeal**
457/8/96	Consultant Physician v Rosemont	Reference to methadone in "Juice"	No breach	No appeal
458/8/96	GP v Sandoz	Disease area campaign to the public	No breach	No appeal
460/9/96	**Serono v Britannia**	**Promotion of Alec**	**Breach 4.1**	**No appeal**
461/9/96	**Yamanouchi v Bioglan**	**Promotion of Benzamycin**	**Breach 7.2 & 10.1**	**No appeal**
462/9/96	**Pharmacist v Bioglan**	**Cocois journal advertisement**	**Breach 7.2**	**No appeal**
464/9/96	**Director/Paragraph 16 v Leo**	**Dovonex competition**	**Breach 18.1**	**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).